

01/203506
Att #16

Search Results - Record(s) 1 through 88 of 88 returned.

1. Document ID: US 6008014 A
Entry 1 of 88

File: USPT

Dec 28, 1999

US-PAT-NO: 6008014

DOCUMENT-IDENTIFIER: US 6008014 A

TITLE: Method of making lipid metabolic pathway compositions

DATE-ISSUED: December 28, 1999

INVENTOR-INFORMATION:
NAME

CITY	STATE	ZIP CODE	COUNTRY
Jimeno; Carlos J.	MA	N/A	N/A
Boston			
Acton; Susan	MA	N/A	N/A
Jamaica Plain			

US-CL-CURRENT: 435/69.1; 435/325, 435/455, 435/91.1, 536/23.1

ABSTRACT:

The present invention relates to the discovery of novel genes encoding Lipid Metabolic Pathway (LMP) polypeptides. Therapeutics, diagnostics and screening assays based on these molecules are also disclosed.
29 Claims, 4 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 4

2. Document ID: US 6004941 A
Entry 2 of 88

File: USPT

Dec 21, 1999

US-PAT-NO: 6004941

DOCUMENT-IDENTIFIER: US 6004941 A

TITLE: Methods for regulating gene expression

DATE-ISSUED: December 21, 1999

INVENTOR-INFORMATION:
NAME

CITY	STATE	ZIP CODE	COUNTRY
Bujard; Hermann	HEidelberg	N/A	DEX
Gossen; Manfred	El Cerrito	CA	N/A

US-CL-CURRENT: 514/44; 424/93.21, 435/320.1, 435/325, 435/455, 435/69.1, 435/70.1, 536/23.4, 536/24.1

ABSTRACT:

Methods of regulating gene expression in subjects using tetracycline-responsive fusion proteins are disclosed. In one embodiment, the method involves introducing into a cell the subject a nucleic acid molecule encoding a fusion protein which activates transcription, the fusion protein comprising a first polypeptide which binds to a tet operator sequence in the presence of tetracycline or a tetracycline analogue operatively linked to a second polypeptide which activates transcription in eukaryotic cells; and modulating the concentration of a tetracycline, or analogue thereof, in the subject. In another embodiment, the cell further comprises a fusion protein which inhibits transcription, the fusion protein comprising a first polypeptide which binds to a tet operator sequence, operatively linked to a second polypeptide which inhibits transcription in eukaryotic cells. In yet another embodiment, the method involves obtaining a cell from a subject, introducing into the cell a first nucleic acid molecule which operatively links a gene to at least one tet operator sequence, introducing into the cell a second nucleic acid molecule encoding a fusion protein of the invention to form a modified cell, administering the modified cell to the subject and modulating the concentration of a tetracycline, or analogue thereof, in the subject. The first and second nucleic acid molecules can be linked or can be separate molecules.
40 Claims, 16 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 15

3. Document ID: US 6001619 A
Entry 3 of 88

File: USPT

Dec 14, 1999

US-PAT-NO: 6001619

DOCUMENT-IDENTIFIER: US 6001619 A

TITLE: Ubiquitin ligases, and uses related thereto

DATE-ISSUED: December 14, 1999

INVENTOR-INFORMATION:
NAME

CITY	STATE	ZIP CODE	COUNTRY
Beach; David	Huntington Bay	NY	N/A
Caligiuri; Maureen G.	Huntington	NY	N/A
Nefsky; Bradley	Highland Park	NJ	N/A

US-CL-CURRENT: 435/193; 536/23.2

ABSTRACT:

The present invention relates to the discovery in eukaryotic cells of a ubiquitin ligases. These proteins are referred to herein collectively as "pub" proteins for Protein Ubiquitin ligase, and individually as h-pub1, h-pub2 and s-pub1 for the human pub1 and pub2 and Schizosaccharomyces pombe pub1 clones, respectively. Pub1 proteins apparently play a role in the ubiquitination of the mitotic activating tyrosine phosphatase cdc25, and thus they may regulate the progression of proliferation in eukaryotic cells by activating the cyclin dependent kinase complexes. In S. pombe, disruption of s-pub1 elevates the level of cdc25 protein in vivo increasing the activity of the tyrosine kinases, wee1 and mik1, required to arrest the cell-cycle. Loss of wee1 function in an S. pombe cell carrying a disruption in the s-pub1 gene results in a lethal premature entry into mitosis; such lethal phenotype can be rescued by the loss of cdc25 function. An ubiquitin thioester adduct of s-pub1 can be isolated from S. pombe and disruption of s-pub1 dramatically reduces ubiquitination of cdc25.

33 Claims, 0 Drawing figures
Exemplary Claim Number: 1

4. Document ID: US 5998174 A
Entry 4 of 88

File: USPT

Dec 7, 1999

US-PAT-NO: 5998174
DOCUMENT-IDENTIFIER: US 5998174 A

TITLE: Multigene vectors

DATE-ISSUED: December 7, 1999

INVENTOR-INFORMATION:
NAME

	CITY	STATE	ZIP CODE	COUNTRY
Glorioso; Joseph C.	Cheswick	PA	N/A	N/A
Krisky; David	Pittsburgh	PA	N/A	N/A

US-CL-CURRENT: 435/91.4; 435/320.1, 435/455, 435/463, 435/465, 435/91.41, 435/91.42, 435/91.5, 536/23.7, 536/23.72

ABSTRACT:

The present invention provides a method for preparing HSV vectors. The method comprises co-transfecting a source vector and a mutating cassette together into a population of appropriate host cells, such that homologous recombination occurs between the mutating cassette and the source vector whereby the mutating cassette replaces a region of the HSV genome. The mutating

cassette has a unique restriction site not present in the sequence of the vector. The method further comprises plaquing the co-transfected host cells, selecting plaques in which recombination has occurred between the source vector and the mutating cassette, and isolating the viral DNA from the plaques. The isolated viral DNA is digested with a restriction endonuclease appropriate for cleaving the viral DNA at the unique restriction site within the mutating cassette to produce two viral polynucleotides. Following purification, the two viral polynucleotides can be ligated to form an HSV vector comprising the two viral polynucleotides. Alternatively, the two isolated viral polynucleotides can be recombined with an insertion cassette to form an HSV vector comprising the insertion cassette at the former locus of the unique restriction site. The present invention further provides a mutant vector, particularly an HSV vector constructed in accordance with the method for the present invention. The present invention further provides a multigene HSV vector, particularly a multigene HSV vector for cancer therapy.

11 Claims, 15 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 15

5. Document ID: US 5994503 A
Entry 5 of 88

File: USPT

Nov 30, 1999

US-PAT-NO: 5994503
DOCUMENT-IDENTIFIER: US 5994503 A

TITLE: Nucleotide and protein sequences of lats genes and methods based thereon

DATE-ISSUED: November 30, 1999

INVENTOR-INFORMATION:
NAME

	CITY	STATE	ZIP CODE	COUNTRY
Xu; Tian	Guilford	CT	N/A	N/A
Tao; Wufan	Branford	CT	N/A	N/A
Wang; Weiji	New Haven	CT	N/A	N/A
Zhang; Sheng	New Haven	CT	N/A	N/A
Yu; Wan	Guilford	CT	N/A	N/A

US-CL-CURRENT: 530/350; 435/194, 435/7.1, 435/925, 530/300, 530/324, 530/325, 530/326

ABSTRACT:

The present invention relates to a tumor suppressor gene, termed large tumor suppressor (lats), and methods for identifying tumor suppressor genes. The method provides nucleotide sequences of lats genes, and amino acid sequences of their encoded proteins, as well as derivatives (e.g., fragments) and analogs thereof. In a specific embodiment, the lats protein is a human protein. The invention further relates to fragments (and derivatives and analogs thereof) of lats which comprise one or more domains of a lats protein. Antibodies to lats, its derivatives and analogs, are additionally provided. Methods of production of the lats proteins, derivatives and analogs, e.g., by recombinant means, are also provided. Therapeutic and diagnostic methods and pharmaceutical compositions are provided. The invention also relates to recombinant plants and animals and methods of increasing the growth of edible plants and animals. In specific examples, isolated lats genes, from Drosophila, mouse, and human, and the sequences thereof, are provided. 67 Claims, 15 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 43

6. Document ID: US 5994070 A
Entry 6 of 88

File: USPT

Nov 30, 1999

US-PAT-NO: 5994070
DOCUMENT-IDENTIFIER: US 5994070 A

TITLE: Trio molecules and uses related thereto

DATE-ISSUED: November 30, 1999

INVENTOR-INFORMATION:
NAME

	CITY	STATE	ZIP CODE	COUNTRY
Streuli, Michel	Brookline	MA	N/A	N/A
Debant, Anne	Padres le Lez	N/A	N/A	FRX
Serra-Pages, Carles	Boston	MA	N/A	N/A

US-CL-CURRENT: 435/6; 435/320.1, 435/325, 435/69.1, 536/23.5, 536/24.31

ABSTRACT:

Nucleic acids encoding TRIO proteins, the TRIO proteins themselves, and active portions thereof as described. In addition, antibodies immunoreactive with TRIO proteins, and preparations of such

compositions are provided. Diagnostic and therapeutic assays and reagents for detecting and treating disorders involving, for example, aberrant expression (or loss thereof) of the TRIO protein are described. Assays are provided for identifying agents that modulate the biological function of TRIO proteins. 25 Claims, 50 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 27

7. Document ID: US 5989804 A
Entry 7 of 88

File: USPT

Nov 23, 1999

US-PAT-NO: 5989804
DOCUMENT-IDENTIFIER: US 5989804 A

TITLE: E6 binding proteins

DATE-ISSUED: November 23, 1999

INVENTOR-INFORMATION:
NAME

	CITY	STATE	ZIP CODE	COUNTRY
Androphy, Elliot J.	Natick	MA	N/A	N/A
Chen, Jason J.	Boston	MA	N/A	N/A

US-CL-CURRENT: 435/5; 435/7.23, 435/7.6, 435/7.7, 435/7.71, 435/7.72, 435/7.92, 514/12, 530/300, 530/350, 536/23.5, 536/23.72, 930/220

ABSTRACT:

E6-BP polypeptides, nucleic acids encoding E6-BP polypeptides, and uses thereof. 10 Claims, 3 Drawing figures Exemplary Claim Number: 1,7 Number of Drawing Sheets: 3

8. Document ID: US 5986054 A
Entry 8 of 88

File: USPT

Nov 16, 1999

US-PAT-NO: 5986054
DOCUMENT-IDENTIFIER: US 5986054 A

TITLE: Genetic sequences and proteins related to alzheimer's disease

DATE-ISSUED: November 16, 1999

INVENTOR-INFORMATION:
NAME

	CITY	STATE	ZIP CODE	COUNTRY
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Rommens; Johanna M.	Toronto	N/A	N/A	CAX
Fraser; Paul E.	Toronto	N/A	N/A	CAX

US-CL-CURRENT: 530/350; 435/69.1

ABSTRACT:

The present invention describes the identification, isolation and cloning of two human presenilin genes, PS-1 and PS-2, mutations in which lead to Familial Alzheimer's Disease. Also identified are presenilin homologue genes in mice, *C. elegans* and *D. melanogaster*. Transcripts and products of these genes are useful in detecting and diagnosing Alzheimer's disease, developing therapeutics for treatment of Alzheimer's disease, as well as the isolation and manufacture of the protein and the constructions of transgenic animals expressing the mutant genes.

29 Claims, 11 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 12

9. Document ID: US 5981702 A
Entry 9 of 88

File: USPT

Nov 9, 1999

US-PAT-NO: 5981702
DOCUMENT-IDENTIFIER: US 5981702 A

TITLE: Cyclin/CDK associated proteins, and uses related thereto

DATE-ISSUED: November 9, 1999

INVENTOR-INFORMATION:
NAME

	CITY	STATE	ZIP CODE	COUNTRY
Zhang; Hui	Huntington Station	NY	N/A	N/A
Beach; David	Huntington Bay	NY	N/A	N/A

US-CL-CURRENT: 530/350

ABSTRACT:

The present invention relates to the discovery in mammalian cells, particularly human cells, of novel S-phase kinase associated proteins, p19 and p45, referred to herein as "Skp". As described herein, these proteins are components of the tumor cell-specific cyclin

A/CDK2 complex and function to facilitate DNA replication. Interference with p45 function in vivo prevented entry into S-phase in both normal and transformed cells. Binding data indicated that p45 and p19 associate with each other in a binary complex. Moreover, p45 is required for p19 binding to cyclin A/CDK2.

13 Claims, 0 Drawing figures
Exemplary Claim Number: 1

10. Document ID: US 5968821 A
Entry 10 of 88

File: USPT

Oct 19, 1999

US-PAT-NO: 5968821
DOCUMENT-IDENTIFIER: US 5968821 A

TITLE: Cell-cycle regulatory proteins, and uses related thereto

DATE-ISSUED: October 19, 1999

INVENTOR-INFORMATION:
NAME

	CITY	STATE	ZIP CODE	COUNTRY
Beach; David H.	Huntington Bay	NY	N/A	N/A
Demetrick; Douglas J.	E. Northport	NY	N/A	N/A
Serrano; Manuel	Mill Neck	NY	N/A	N/A
Hannon; Gregory J.	Huntington	NY	N/A	N/A

US-CL-CURRENT: 435/325; 435/320.1, 435/455, 435/6, 435/69.1, 536/23.1

ABSTRACT:

The present invention relates to the discovery in eukaryotic cells, particularly mammalian cells, of a novel family of cell-cycle regulatory proteins ("CCR-proteins"). As described herein, this family of proteins includes a polypeptide having an apparent molecular weight of 16 kDa, and a polypeptide having an apparent molecular weight of approximately 15 kDa, each of which can function as an inhibitor of cell-cycle progression, and therefore ultimately of cell growth.

Thus, similar to the role of p21 to the p53 checkpoint, the subject CCR-proteins may function coordinately with the cell-cycle regulatory protein, retinoblastoma (RB). Furthermore, the CCR-protein family includes a protein having an apparent molecular weight of 13.5 kDa (hereinafter "p13.5"). The presumptive role of p13.5, like p16 and p15, is in the regulation of the cell-cycle.

35 Claims, 11 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 11

11. Document ID: US 5965791 A
Entry 11 of 88

File: USPT

Oct 12, 1999

US-PAT-NO: 5965791
DOCUMENT-IDENTIFIER: US 5965791 A

TITLE: Vector for introducing a gene into a plant, and methods for
producing transgenic plants
and multitudinously introducing genes into a plant using the vector

DATE-ISSUED: October 12, 1999

INVENTOR-INFORMATION:
NAME

	CITY	STATE	ZIP CODE	COUNTRY
Ebinuma; Hiroyasu	Tokyo	N/A	N/A	JPX
Sugita; Koichi	Tokyo	N/A	N/A	JPX
Matsunaga; Etsuko	Tokyo	N/A	N/A	JPX
Yamakado; Mikiko	Tokyo	N/A	N/A	JPX

ABSTRACT:

A vector for introducing a desired gene into a planet, which comprises the desired gene and at least one morphological abnormally induction (MAI) gene as a marker gene, or which comprises the desired gene, at least one MAI gene and a removable element. A method for producing a transgenic plant free from the influence of a marker gene. A method for multitudinously introducing desired genes into one plant.
30 Claims, 29 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 29

12. Document ID: US 5965790 A
Entry 12 of 88

File: USPT

Oct 12, 1999

US-PAT-NO: 5965790
DOCUMENT-IDENTIFIER: US 5965790 A

TITLE: SR-BI regulatory sequences and therapeutic methods of use

DATE-ISSUED: October 12, 1999

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Acton; Susan Laurene

Lexington

MA

N/A

N/A

US-CL-CURRENT: 800/18; 435/29, 435/320.1, 435/325, 435/6, 536/24.1, 536/24.31, 800/21

ABSTRACT:

The invention features nucleic acid molecules that are involved with (e.g. activate or regulate) human SR-BI receptor transcription, as well as complements thereto, and homologs thereof. In addition, drug discovery assays are provided for identifying agents which modulate SR-BI promoter activity and thereby modulate the expression of a gene regulated thereby. Such agents can be useful therapeutically for treating or preventing the development of a disease or condition that is caused or contributed to by an aberrant SR-BI activity. In a preferred embodiment, the disease or condition is characterized by inappropriate lipid transfer or metabolism (e.g., atherosclerosis or gallstone formation). Such agents can also be used to modulate expression of a specific gene under the control of the SR-BI promoter in gene therapy. Moreover, the present invention provides diagnostic assays and reagents for determining whether a subject has a disorder involving, for example, aberrant expression of SR-BI genes.
31 Claims, 3 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 3

13. Document ID: US 5962316 A
Entry 13 of 88

File: USPT

Oct 5, 1999

US-PAT-NO: 5962316
DOCUMENT-IDENTIFIER: US 5962316 A

TITLE: Cell-cycle regulatory proteins, and uses related thereto

DATE-ISSUED: October 5, 1999

INVENTOR-INFORMATION:

	CITY	STATE	ZIP CODE	COUNTRY
Beach; David H.	Huntington Bay	NY	N/A	N/A
Demetrick; Douglas J.	Northport	NY	N/A	N/A
Serrano; Manuel	Mill Neck	NY	N/A	N/A

Hannon; Gregory J.

Huntington

NY

N/A

N/A

US-CL-CURRENT: 435/325; 424/185.1, 424/93.21, 435/320.1, 435/455, 435/6, 435/69.1, 514/44, 530/350, 536/23.1, 536/23.4, 536/23.5, 536/24.1

ABSTRACT:

The present invention relates to the discovery in eukaryotic cells, particularly mammalian cells, of a novel family of cell-cycle regulatory proteins ("CCR-proteins"). As described herein, this family of proteins includes a polypeptide having an apparent molecular weight of 16 kDa, and a polypeptide having an apparent molecular weight of approximately 15 kDa, each of which can function as an inhibitor of cell-cycle progression, and therefore ultimately of cell growth.

Thus, similar to the role of p21 to the p53 checkpoint, the subject CCR-proteins may function coordinately with the cell-cycle regulatory protein, retinoblastoma (RB). Furthermore, the

CCR-protein family includes a protein having an apparent molecular weight of 13.5 kDa

(hereinafter "p13.5"). The presumptive role of p13.5, like p16 and p15, is in the regulation of the cell-cycle.

40 Claims, 11 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 11

14. Document ID: US 5955306 A

Entry 14 of 88

File: USPT

Sep 21, 1999

US-PAT-NO: 5955306

DOCUMENT-IDENTIFIER: US 5955306 A

TITLE: Genes encoding proteins that interact with the tub protein

DATE-ISSUED: September 21, 1999

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Gimeno; Carlos J.

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MA

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N/A

N/A

US-CL-CURRENT: 435/69.1; 435/252.3, 435/254.11, 435/320.1, 435/325, 435/71.1, 536/23.5, 536/24.3, 536/24.31

ABSTRACT:

The present invention relates to the discovery of novel genes encoding Tub interactor (TI) polypeptides. Therapeutics, diagnostics and screening assays based on

these molecules are also disclosed.

23 Claims, 6 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 15

15. Document ID: US 5948653 A

Entry 15 of 88

File: USPT

Sep 7, 1999

US-PAT-NO: 5948653

DOCUMENT-IDENTIFIER: US 5948653 A

TITLE: Sequence alterations using homologous recombination

DATE-ISSUED: September 7, 1999

INVENTOR-INFORMATION:

NAME

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STATE

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COUNTRY

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N/A

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N/A

US-CL-CURRENT: 435/6; 435/470, 435/471, 435/490, 435/91.1, 435/DIG37, 435/DIG5, 435/DIG6, 435/DIG8, 530/350, 536/23.1

ABSTRACT:

The invention relates to methods for targeting an exogenous polynucleotide or exogenous

complementary polynucleotide pair to a predetermined endogenous DNA target sequence in a target

cell by homologous pairing, particularly for altering an endogenous DNA sequence, such as a

chromosomal DNA sequence, typically by targeted homologous recombination. In certain embodiments,

the invention relates to methods for targeting an exogenous polynucleotide having a linked

chemical substituent to a predetermined endogenous DNA sequence in a metabolically active target

cell, generating a DNA sequence-specific targeting of one or more chemical substituents in an intact nucleus of a metabolically active target cell, generally for purposes of altering a

predetermined endogenous DNA sequence in the cell. The invention also relates to compositions

that contain exogenous targeting polynucleotides, complementary pairs of exogenous targeting

polynucleotides, chemical substituents of such polynucleotides, and recombinase proteins used in

the methods of the invention.

40 Claims, 43 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 24

16. Document ID: US 5945339 A

Entry 16 of 88

File: USPT

Aug 31, 1999

US-PAT-NO: 5945339
DOCUMENT-IDENTIFIER: US 5945339 A

TITLE: Methods to promote homologous recombination in eukaryotic cells and organisms

DATE-ISSUED: August 31, 1999

INVENTOR-INFORMATION:
NAME

CITY

STATE

ZIP CODE

COUNTRY

Holloman; William K.

Yorktown Heights

NY

N/A

N/A

Kniec; Eric B.

Malvern

PA

N/A

N/A

US-CL-CURRENT: 435/477; 435/483, 435/484

ABSTRACT:

The invention concerns genes encoding recombinases that can be used to promote homologous recombination in eukaryotic cells. The application teaches methods by which a recombinase of one species can be used to isolate a homologous recombinase of a different species and methods to identify the isolated homologs. Recombinases from *Ustilago maydis*, *Saccharomyces cerevisiae* and humans are specifically included in the invention.

The invention encompasses the method of producing an isolated recombinase protein in a prokaryotic cell and recovering the product in an active form. The invention also encompasses a genetically engineered gene which encodes a non-naturally occurring recombinase that causes a greater rate of recombination than does the naturally occurring recombinase. The invention further encompasses the use of recombinase proteins and of recombinase genes to promote homologous recombination, including recombination between a host cell genome and a chimeric oligonucleotide, i.e., an oligonucleotide having both RNA and DNA bases. 6 Claims, 14 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 10

17. Document ID: US 5925558 A
Entry 17 of 88

File: USPT

Jul 20, 1999

US-PAT-NO: 5925558
DOCUMENT-IDENTIFIER: US 5925558 A

TITLE: Assays for protein kinases using fluorescent protein substrates

DATE-ISSUED: July 20, 1999

INVENTOR-INFORMATION:
NAME

CITY

STATE

ZIP CODE
COUNTRY

Tsien; Roger Y.

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N/A

N/A

Cubitt; Andrew B.

San Diego

CA

N/A

N/A

US-CL-CURRENT: 435/252.3; 435/320.1, 435/325, 435/440, 536/23.1, 536/23.4

ABSTRACT:

This invention provides assays for protein kinase activity using fluorescent proteins engineered to include sequences that can be phosphorylated by protein kinases. The proteins exhibit different fluorescent properties in the non-phosphorylated and phosphorylated states. 23 Claims, 14 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 14

18. Document ID: US 5922927 A
Entry 18 of 88

File: USPT

Jul 13, 1999

US-PAT-NO: 5922927
DOCUMENT-IDENTIFIER: US 5922927 A

TITLE: Methods for producing tetracycline-regulated transgenic mice

DATE-ISSUED: July 13, 1999

INVENTOR-INFORMATION:
NAME

CITY

STATE

ZIP CODE

COUNTRY

Bujard; Hermann

Heidelberg

N/A

N/A

DEX

Gossen; Manfred

Heidelberg

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DEX

Salfeld; Jochen G.

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MA

N/A

N/A

Voss; Jeffrey W.

Framingham

MA

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N/A

US-CL-CURRENT: 800/25; 435/320.1, 435/325, 435/455, 435/463, 435/69.1, 800/18, 800/22

ABSTRACT:

Transgenic mice carrying two transgenes, the first coding for a

transactivator fusion protein
 comprising a tet repressor and a polypeptide which directly or indirectly
 activates in eucaryotic
 cells, and the second comprising a gene operably linked to a minimal
 promoter operably linked to
 at least one tet operator sequence, are disclosed. Isolated DNA molecules
 (e.g., targeting
 vectors) for integrating a polynucleotide sequence encoding a transactivator
 of the invention at
 a predetermined location within a second target DNA molecule by
 homologous recombination are also
 disclosed. Transgenic mice having the DNA molecules of the invention
 integrated at a
 predetermined location in a chromosome by homologous recombination are
 also encompassed by the
 invention. Methods to regulate the expression of a tet operator linked-gene
 of interest by
 administering tetracycline or a tetracycline analogue to a mouse of the
 invention are also
 disclosed. The regulatory system of the invention allows for conditional
 inactivation or
 modulation of expression of a gene of interest in a host cell or mouse.
 11 Claims, 3 Drawing figures
 Exemplary Claim Number: 1,2
 Number of Drawing Sheets: 32

19. Document ID: US 5919997 A

Entry 19 of 88

File: USPT

Jul 6, 1999

US-PAT-NO: 5919997

DOCUMENT-IDENTIFIER: US 5919997 A

TITLE: Transgenic mice having modified cell-cycle regulation

DATE-ISSUED: July 6, 1999

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Beach; David H.

Huntington Bay

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Serrano; Manuel

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N/A

N/A

DePinho; Ronald A.

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N/A

N/A

US-CL-CURRENT: 800/18; 424/9.2, 435/320.1, 435/325, 435/455,
 435/463, 435/467, 435/91.2, 800/22,
 800/25, 800/3

ABSTRACT:

The present invention relates to transgenic mice in which the biological
 function of at least one
 cell cycle regulatory proteins of the INK4 family is altered.

11 Claims, 3 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 2

20. Document ID: US 5912411 A

Entry 20 of 88

File: USPT

Jun 15, 1999

US-PAT-NO: 5912411

DOCUMENT-IDENTIFIER: US 5912411 A

TITLE: Mice transgenic for a tetracycline-inducible transcriptional activator

DATE-ISSUED: June 15, 1999

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Bujard; Hermann

Heidelberg

N/A

N/A

DEX

Gossen; Manfred

El Cerrito

CA

N/A

N/A

US-CL-CURRENT: 800/18; 435/325, 435/462, 435/463, 435/69.1,
 435/70.1, 514/152, 536/23.4, 536/24.1

ABSTRACT:

Transgenic mice carrying a transgene comprising a nucleic acid molecule
 encoding protein useful
 for regulating the expression of genes in eukaryotic cells in a highly
 controlled manner are
 disclosed. In the regulatory system of the invention, transcription of a tet
 operator-linked
 nucleotide sequence is stimulated by a transcriptional activator fusion
 protein composed of two
 polypeptides, a first polypeptide which binds to tet operator sequences in
 the presence of
 tetracycline operatively linked to a second polypeptide activates
 transcription in eukaryotic
 cells. In a preferred embodiment, the transgene encoding the transcriptional
 activator fusion
 protein is integrated at a predetermined location within the chromosome of
 the transgenic mouse.

36 Claims, 18 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 15

21. Document ID: US 5912326 A

Entry 21 of 88

File: USPT

Jun 15, 1999

US-PAT-NO: 5912326

DOCUMENT-IDENTIFIER: US 5912326 A

TITLE: Cerebellum-derived growth factors

DATE-ISSUED: June 15, 1999

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Chang; Han

Mountain View

CA

N/A

N/A

US-CL-CURRENT: 530/399; 530/350

ABSTRACT:

The present invention relates to the discovery of a novel erbB receptor ligand, referred to hereinafter as "cdGF", which protein has apparently broad involvement in the formation and maintenance of ordered spatial arrangements of differentiated tissues in vertebrates, and can be used to generate and/or maintain an array of different vertebrate tissue both in vitro and in vivo.

11 Claims, 2 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 1

22. Document ID: US 5912137 A

Entry 22 of 88

File: USPT

Jun 15, 1999

US-PAT-NO: 5912137

DOCUMENT-IDENTIFIER: US 5912137 A

TITLE: Assays for protein kinases using fluorescent

DATE-ISSUED: June 15, 1999

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Tsien; Roger Y.

La Jolla

CA

N/A

N/A

Cubitt; Andrew B.

San Diego

CA

N/A

N/A

US-CL-CURRENT: 435/15; 530/350; 530/352; 536/23.4

ABSTRACT:

This invention provides assays for protein kinase activity using fluorescent proteins engineered to include sequences that can be phosphorylated by protein kinases. The proteins exhibit different fluorescent properties in the non-phosphorylated and phosphorylated states.

24 Claims, 14 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 14

23. Document ID: US 5910415 A

Entry 23 of 88

File: USPT

Jun 8, 1999

US-PAT-NO: 5910415

DOCUMENT-IDENTIFIER: US 5910415 A

TITLE: Controlled modification of eukaryotic genomes

DATE-ISSUED: June 8, 1999

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Hodges; Thomas K.

West Lafayette

IN

N/A

N/A

Lyznik; Leszek A.

Johnston

IA

N/A

N/A

US-CL-CURRENT: 435/6; 435/320.1; 435/410; 536/23.1; 800/266; 800/267; 800/278

ABSTRACT:

A method of using a unique DNA construct for the creation of transgenic eukaryotic cells is

described. The method allows a more precise and effective transformation procedure that targets

the insertion of a DNA sequence into a predetermined DNA locus, while enabling the removal of any

randomly inserted DNA sequences that occur as a by product of known transformation procedures.

12 Claims, 18 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 11

24. Document ID: US 5888981 A

Entry 24 of 88

File: USPT

Mar 30, 1999

US-PAT-NO: 5888981

DOCUMENT-IDENTIFIER: US 5888981 A

TITLE: Methods for regulating gene expression

DATE-ISSUED: March 30, 1999

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Bujard; Hermann

Heidelberg

N/A

N/A

DEX

Gossen; Manfred

El Cerrito

CA

N/A

N/A

Salfeld; Jochen G.

North Grafton

MA

N/A

N/A

Voss, Jeffrey W.

West Boylston

MA

N/A

N/A

US-CL-CURRENT: 514/44; 424/93.21, 435/455, 435/463, 435/465

ABSTRACT:

A method for regulating expression of a tet operator-linked gene in a cell of a subject is disclosed. In one embodiment, the method involves introducing into the cell a nucleic acid molecule encoding a tetracycline-controllable transactivator (tTA), the tTA comprising a Tet repressor operably linked to a polypeptide which directly or indirectly activates transcription in eucaryotic cells; and modulating the concentration of a tetracycline, or analogue thereof, in the subject. Alternatively, in another embodiment, the method involves obtaining the cell from the subject, introducing into the cell a first nucleic acid molecule which operatively links a gene to at least one tet operator sequence, introducing into the cell a second nucleic acid molecule encoding a tTA, to form a modified cell, administering the modified cell to the subject, and modulating the concentration of a tetracycline, or analogue thereof, in the subject.

The first and second nucleic acid molecule can be within a single molecule (e.g., in the same vector) or on separate molecules.

17 Claims, 36 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 32

25. Document ID: US 5888732 A

Entry 25 of 88

File: USPT

Mar 30, 1999

US-PAT-NO: 5888732

DOCUMENT-IDENTIFIER: US 5888732 A

TITLE: Recombinational cloning using engineered recombination sites

DATE-ISSUED: March 30, 1999

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Hartley, James L.

Frederick

MD

N/A

N/A

Brasch, Michael A.

Gaithersburg

MD

N/A

N/A

US-CL-CURRENT: 435/6; 435/320.1, 435/91.42, 536/23.1, 536/24.2

ABSTRACT:

Recombinational cloning is provided by the use of nucleic acids, vectors and methods, in vitro and in vivo, for moving or exchanging segments of DNA molecules using

engineered recombination

sites and recombination proteins to provide chimeric DNA molecules that have the desired

characteristic(s) and/or DNA segment(s).

47 Claims, 44 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 44

26. Document ID: US 5885776 A

Entry 26 of 88

File: USPT

Mar 23, 1999

US-PAT-NO: 5885776

DOCUMENT-IDENTIFIER: US 5885776 A

TITLE: Glaucoma compositions and therapeutic and diagnostic uses therefor

DATE-ISSUED: March 23, 1999

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Stone, Edwin M.

Iowa City

IA

N/A

N/A

Sheffield, Val C.

Coralville

IA

N/A

N/A

Alward, Wallace L. M.

Iowa City

IA

N/A

N/A

US-CL-CURRENT: 435/6

ABSTRACT:

Methods and compositions for treating glaucoma; and glaucoma diagnostics are disclosed.

37 Claims, 10 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 6

27. Document ID: US 5882888 A

Entry 27 of 88

File: USPT

Mar 16, 1999

US-PAT-NO: 5882888

DOCUMENT-IDENTIFIER: US 5882888 A

TITLE: DNA integration by transposition

DATE-ISSUED: March 16, 1999

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

J.o slashed.rgensen; Steen Troels

Aller.o slashed.d

N/A

N/A

DKX

US-CL-CURRENT: 435/69.1; 435/243, 435/252.31, 435/320.1, 435/473, 435/477, 435/478, 435/489, 435/91.4, 536/23.1, 536/24.2

ABSTRACT:

Multicopy strains of gram-positive bacteria carrying multiple copies of a DNA sequence of interest may be constructed by use of a method involving introduction of a DNA construct comprising the DNA sequence of interest into the genome of the recipient cell by transposition and subsequent deletion of a marker gene used for selection of the cells having received the DNA construct by a resolution system. The multicopy strains are preferably free from a gene encoding an undesirable marker such as an antibiotic resistance marker.
6 Claims, 31 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 31

28. Document ID: US 5874283 A

Entry 28 of 88

File: USPT

Feb 23, 1999

US-PAT-NO: 5874283

DOCUMENT-IDENTIFIER: US 5874283 A

TITLE: Mammalian flap-specific endonuclease

DATE-ISSUED: February 23, 1999

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Harrington; John Joseph

Shaker Heights

OH

44120

N/A

Hsieh; Chih-Lin

St. Louis

MO

63131

N/A

Lieber; Michael R.

St. Louis

MO

63131

N/A

US-CL-CURRENT: 435/252.3; 435/199, 435/252.33, 435/320.1, 435/69.1, 530/350, 536/23.2, 536/23.5

ABSTRACT:

Compositions comprising human FEN-1(flap) endonucleases, nucleic acids encoding them, and methods for their use are provided.
6 Claims, 12 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 7

29. Document ID: US 5869239 A

Entry 29 of 88

File: USPT

Feb 9, 1999

US-PAT-NO: 5869239

DOCUMENT-IDENTIFIER: US 5869239 A

TITLE: Library screening method

DATE-ISSUED: February 9, 1999

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Treco; Douglas A.

Arlington

MA

N/A

N/A

Miller; Allan M.

Medford

MA

N/A

N/A

US-CL-CURRENT: 435/6; 435/477, 435/482, 435/490, 435/91.4, 435/91.41

ABSTRACT:

Materials and methods for homologous-recombination screening of DNA libraries constructed in a eukaryotic host and methods for homologous-recombination chromosome walking for isolating overlapping DNA sequences for building an extended physical map of a chromosomal region.
41 Claims, 18 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 17

30. Document ID: US 5866755 A

Entry 30 of 88

File: USPT

Feb 2, 1999

US-PAT-NO: 5866755

DOCUMENT-IDENTIFIER: US 5866755 A

TITLE: Animals transgenic for a tetracycline-regulated transcriptional inhibitor

DATE-ISSUED: February 2, 1999

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Bujard; Hermann

Heidelberg

N/A

N/A

DEX

Gossen; Manfred

El Cerrito

CA

N/A

N/A

US-CL-CURRENT: 800/9; 800/18

ABSTRACT:

Transgenic animals carrying a transgene comprising a nucleic acid molecule encoding protein useful for regulating the expression of genes in eukaryotic cells and organisms in a highly controlled manner are disclosed. In the regulatory system of the invention, transcription of a tet operator-linked nucleotide sequence is inhibited by a transcriptional inhibitor fusion

protein composed of two polypeptides, a first polypeptide which binds to tet operator sequences and a second polypeptide which directly or indirectly inhibits transcription in eukaryotic cells.

In various embodiment, the first polypeptide binds to tet operator sequences either: (i) in the absence but not the presence of tetracycline (or an analogue thereof) or (ii) in the presence but not the absence of tetracycline (or an analogue thereof). In a preferred embodiment, the

transgene encoding the transcriptional inhibitor fusion protein is integrated at a predetermined location within the chromosome of the transgenic animal.

25 Claims, 18 Drawing figures

Exemplary Claim Number: 1,2,3

Number of Drawing Sheets: 15

31. Document ID: US 5859310 A
Entry 31 of 88

File: USPT

Jan 12, 1999

US-PAT-NO: 5859310

DOCUMENT-IDENTIFIER: US 5859310 A

TITLE: Mice transgenic for a tetracycline-controlled transcriptional activator

DATE-ISSUED: January 12, 1999

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Bujard; Hermann

Heidelberg

N/A

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Gossen; Manfred

El Cerrito

CA

N/A

N/A

Salfeld; Jochen G.

Noth Graton

MA

N/A

N/A

Voss; Jeffrey W.

West Boylson

MA

N/A

N/A

US-CL-CURRENT: 800/9; 435/320.1, 435/325, 435/69.1, 435/70.1, 514/152, 536/23.4, 536/24.1,

800/18, 800/22, 800/25, 800/4

ABSTRACT:

Transgenic mice carrying two transgenes, the first coding for a transactivator fusion protein comprising a tet repressor and a polypeptide which directly or indirectly activates transcription of a tet operator-linked gene in eucaryotic cells, and the second comprising a gene operably linked to a minimal promoter operably linked to at least one tet operator sequence, are disclosed. Isolated DNA molecules (e.g., targeting vectors) for integrating a polynucleotide

sequence encoding a transactivator of the invention at a predetermined location within a second target DNA molecule by homologous recombination are also disclosed.

Transgenic mice having the DNA molecules of the invention integrated at a predetermined location in a chromosome by

homologous recombination are also encompassed by the invention.

Methods to regulate the

expression of a tet operator linked-gene of interest by administering tetracycline or a

tetracycline analogue to a mouse of the invention are also disclosed. The regulatory system of

the invention allows for conditional inactivation or modulation of expression of a gene of

interest in a host cell or mouse.

20 Claims, 36 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 32

32. Document ID: US 5840540 A
Entry 32 of 88

File: USPT

Nov 24, 1998

US-PAT-NO: 5840540

DOCUMENT-IDENTIFIER: US 5840540 A

TITLE: Nucleic acids encoding presenilin II

DATE-ISSUED: November 24, 1998

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

St. George-Hyslop; Peter H.

Toronto

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N/A

CAX

Rommens; Johanna M.

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N/A

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Fraser; Paul E.

Toronto

N/A

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US-CL-CURRENT: 435/69.1; 435/252.3, 435/320.1, 435/325, 530/350, 536/23.1, 536/24.3

ABSTRACT:

The present invention describes the identification, isolation and cloning of two human presenilin

genes, PS-1 and PS-2, mutations in which lead to Familial Alzheimer's Disease. Also identified are presenilin homologue genes in mice, C. elegans and D. melanogaster. Transcripts and products of these genes are useful in detecting and diagnosing Alzheimer's disease, developing therapeutics for treatment of Alzheimer's disease, as well as the isolation and manufacture of the protein and the constructions of transgenic animals expressing the mutant genes.
 31 Claims, 11 Drawing figures
 Exemplary Claim Number: 1
 Number of Drawing Sheets: 10

33. Document ID: US 5830461 A
 Entry 33 of 88

File: USPT

Nov 3, 1998

US-PAT-NO: 5830461
 DOCUMENT-IDENTIFIER: US 5830461 A

TITLE: Methods for promoting wound healing and treating transplant-associated vasculopathy

DATE-ISSUED: November 3, 1998

INVENTOR-INFORMATION:
 NAME

CITY	STATE	ZIP CODE	COUNTRY
Billiar, Timothy R.	Pittsburgh PA	N/A	N/A
Tzeng, Edith	Pittsburgh PA	N/A	N/A
Shears, II, Larry L.	Bethel Park PA	N/A	N/A
Geller, David A.	Pittsburgh PA	N/A	N/A
Edington, Howard David James	Pittsburgh PA	N/A	N/A

US-CL-CURRENT: 424/94.4; 424/94.1, 435/189

ABSTRACT:

The present invention provides a method of promoting the closure of a wound in a patient. This method involves transferring exogenous iNOS to the region of the wound whereby a product of iNOS is produced in the region of the wound to promote the closure of the wound.
 8 Claims, 13 Drawing figures
 Exemplary Claim Number: 1
 Number of Drawing Sheets: 8

34. Document ID: US 5844079 A
 Entry 34 of 88

File: USPT

Dec 1, 1998

US-PAT-NO: 5844079
 DOCUMENT-IDENTIFIER: US 5844079 A

TITLE: Vertebrate embryonic pattern-inducing proteins, and uses related thereto

DATE-ISSUED: December 1, 1998

INVENTOR-INFORMATION:
 NAME

CITY	STATE	ZIP CODE	COUNTRY
Ingham, Philip W.	Summertown N/A	N/A	GB2
McMahon, Andrew P.	Lexington MA	N/A	N/A
Tabin, Clifford J.	Cambridge MA	N/A	N/A

US-CL-CURRENT: 530/350; 435/252.3, 435/320.1, 435/69.1, 435/7.1, 530/300, 536/23.1, 536/23.5

ABSTRACT:

The present invention concerns the discovery that proteins encoded by a family of vertebrate genes, termed here hedgehog-related genes, comprise morphogenic signals produced by embryonic patterning centers, and are involved in the formation of ordered spatial arrangements of differentiated tissues in vertebrates. The present invention makes available compositions and methods that can be utilized, for example to generate and/or maintain an array of different vertebrate tissue both in vitro and in vivo.
 41 Claims, 22 Drawing figures
 Exemplary Claim Number: 1
 Number of Drawing Sheets: 21

35. Document ID: US 5849571 A
 Entry 35 of 88

File: USPT

Dec 15, 1998

US-PAT-NO: 5849571
 DOCUMENT-IDENTIFIER: US 5849571 A

TITLE: Latency active herpes virus promoters and their use

DATE-ISSUED: December 15, 1998

INVENTOR-INFORMATION:
 NAME

CITY	STATE	ZIP CODE	COUNTRY
Glorioso, Joseph C.			

Cheswick	PA	N/A	N/A
Fink; David J.	Pittsburgh	PA	N/A
Goins; William F.	Pittsburgh	PA	N/A

US-CL-CURRENT: 435/320.1; 435/456

ABSTRACT:

The application discloses the structure of a herpes virus promoter that by means of which one can obtain the transcription of a non-herpes gene in a cell latently infected with a herpes virus. An HSV-1 vector comprising a LAP2 promoter encoded by SEQ ID NO:1, or fragments of SEQ ID NO:1 which have LAP 2 promoter activity regulating the expression of a heterologous gene is particularly disclosed. The herpes virus is preferably used to obtain such expression in the neurons of the peripheral nerves, and the ganglion cells of the cranial nerves. The invention teaches that specific diseases and pathological conditions and the corresponding non-herpes genes wherein such expression has practical value.
12 Claims, 9 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6

36. Document ID: US 5834202 A
Entry 36 of 88
File: USPT
Nov 10, 1998

US-PAT-NO: 5834202
DOCUMENT-IDENTIFIER: US 5834202 A

TITLE: Methods for the isothermal amplification of nucleic acid molecules

DATE-ISSUED: November 10, 1998

INVENTOR-INFORMATION:
NAME

	CITY	STATE	ZIP CODE	COUNTRY
Auerbach; Jeffrey I.	Rockville	MD	N/A	N/A

US-CL-CURRENT: 435/6; 435/320.1, 435/91.1, 435/91.2, 536/23.1, 536/24.2, 536/24.33

ABSTRACT:

Methods for amplifying a nucleic acid molecule which employs a single primer, and in which the amplification is performed under isothermal conditions. The invention also includes kits containing reagents for conducting the method.
24 Claims, 19 Drawing figures

Exemplary Claim Number: 1
Number of Drawing Sheets: 19

37. Document ID: US 5849991 A
Entry 37 of 88
File: USPT
Dec 15, 1998

US-PAT-NO: 5849991
DOCUMENT-IDENTIFIER: US 5849991 A

TITLE: Mice homozygous for an inactivated .alpha. 1,3-galactosyl transferase gene

DATE-ISSUED: December 15, 1998

INVENTOR-INFORMATION:
NAME

	CITY	STATE	ZIP CODE	COUNTRY
d'Apice; Anthony J. F.	Balwyn	N/A	N/A	AUX
Pearse; Martin J.	Mordialloc	N/A	N/A	AUX
Robins; Allan J.	Waterloo Corner	N/A	N/A	AUX
Crawford; Robert J.	West Lake Shores	N/A	N/A	AUX
Rathjen; Peter D.	Blackwood	N/A	N/A	AUX

US-CL-CURRENT: 800/8; 435/320.1, 435/354, 435/463, 800/17, 800/18, 800/21, 800/22, 800/24

ABSTRACT:

Human pre-formed xenoantibodies play an important role in the hyperacute rejection response in human xenotransplantation. Disclosed are materials and methods for removing or neutralizing such antibodies. Also disclosed are materials and methods for reducing or eliminating the epitopes in the donor organs that are recognized by such antibodies. Such epitopes are formed as the result of activity by the enzyme .alpha.-1,3 galactosyltransferase. The porcine gene encoding .alpha.-1,3 galactosyltransferase is disclosed, as are materials and methods for inactivating ("knocking out") the .alpha.-1,3 galactosyltransferase gene in mammalian cells and embryos. Included are nucleic acid constructs useful for inactivating the .alpha.-1,3 galactosyltransferase gene in a target cell. Also disclosed is a novel leukemia inhibitory factor (T-LIF) that is useful for maintenance of embryonic stem cells and primordial germ cells in culture.
13 Claims, 47 Drawing figures

Exemplary Claim Number: 5
Number of Drawing Sheets: 42

38. Document ID: US 5849989 A
Entry 38 of 88

File: USPT

Dec 15, 1998

US-PAT-NO: 5849989
DOCUMENT-IDENTIFIER: US 5849989 A

TITLE: Insulin promoter factor, and uses related thereto

DATE-ISSUED: December 15, 1998

INVENTOR-INFORMATION:
NAME

CITY

STATE

ZIP CODE

COUNTRY

Edlund; Thomas

Ume.ang.

N/A

N/A

SEX

US-CL-CURRENT: 800/9; 800/18

ABSTRACT:

The present invention relates to the discovery in eukaryotic cells, particularly mammalian cells, of novel a transcriptional regulatory factor, referred to hereinafter as "Insulin Promoter Factor 1" or "Ipfl".
13 Claims, 4 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 4

39. Document ID: US 5814618 A
Entry 39 of 88

File: USPT

Sep 29, 1998

US-PAT-NO: 5814618
DOCUMENT-IDENTIFIER: US 5814618 A

TITLE: Methods for regulating gene expression

DATE-ISSUED: September 29, 1998

INVENTOR-INFORMATION:
NAME

CITY

STATE

ZIP CODE

COUNTRY

Bujard; Hermann

Heidelberg

N/A

N/A

DEX

Gossen; Manfred

El Cerrito

CA

N/A

N/A

US-CL-CURRENT: 514/44; 424/93.21

ABSTRACT:

Methods of regulating gene expression in subjects using tetracycline-responsive fusion proteins are disclosed. In one embodiment, the method involves introducing into a cell the subject a nucleic acid molecule encoding a fusion protein which inhibits transcription, the fusion protein comprising a first polypeptide which binds to a tet operator sequence, operatively linked to a heterologous second polypeptide which inhibits transcription in eukaryotic cells; and modulating the concentration of a tetracycline, or analogue thereof, in the subject. The first polypeptide can binds to a tet operator sequence in the absence, but not the presence, of tetracycline. Alternatively, the first polypeptide can binds to a tet operator sequence in the presence, but not the absence, of tetracycline. In another embodiment, the method of the invention involves obtaining a cell from a subject, introducing into the cell a first nucleic acid molecule which operatively links a gene to at least one tet operator sequence, introducing into the cell a second nucleic acid molecule encoding an inhibitory fusion protein of the invention to form a modified cell, administering the modified cell to the subject and modulating the concentration of a tetracycline, or analogue thereof, in the subject. The first and second nucleic acid molecules can be linked or can be separate molecules.
30 Claims, 18 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 15

40. Document ID: US 5807708 A
Entry 40 of 88

File: USPT

Sep 15, 1998

US-PAT-NO: 5807708
DOCUMENT-IDENTIFIER: US 5807708 A

TITLE: Conservin nucleic acid molecules and compositions

DATE-ISSUED: September 15, 1998

INVENTOR-INFORMATION:
NAME

CITY

STATE

ZIP CODE

COUNTRY

Falb; Dean A.

Wellesley

MA

N/A

N/A

Gimeno; Carlos J.

Boston

MA

N/A

N/A

US-CL-CURRENT: 435/69.1; 435/252.3, 435/254.11, 435/320.1, 435/325, 536/23.1, 536/23.5

ABSTRACT:

The present invention relates to the discovery of novel conservin genes and polypeptides. Therapeutics, diagnostics and screening assays based on these molecules are also disclosed.
54 Claims, 4 Drawing figures

Exemplary Claim Number: 1
Number of Drawing Sheets: 4

41. Document ID: US 5800998 A
Entry 41 of 88

File: USPT

Sep 1, 1998

US-PAT-NO: 5800998
DOCUMENT-IDENTIFIER: US 5800998 A

TITLE: Assays for diagnosing type II diabetes in a subject

DATE-ISSUED: September 1, 1998

INVENTOR-INFORMATION:
NAME

CITY

STATE

ZIP CODE

COUNTRY

Glucksmann; M. Alexandra

Somerville

MA

N/A

N/A

US-CL-CURRENT: 435/6; 514/44, 536/23.1, 536/23.5

ABSTRACT:

Assays for determining whether a subject has or is at risk for developing type II diabetes, which are based on detecting the presence or absence of alterations in the hepatic nuclear factor 1 (HNF-1) gene or protein of the subject are disclosed.
6 Claims, 1 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 1

42. Document ID: US 5801030 A
Entry 42 of 88

File: USPT

Sep 1, 1998

US-PAT-NO: 5801030
DOCUMENT-IDENTIFIER: US 5801030 A

TITLE: Methods and vectors for site-specific recombination

DATE-ISSUED: September 1, 1998

INVENTOR-INFORMATION:
NAME

CITY

STATE

ZIP CODE

COUNTRY

McVey; Duncan L.

Derwood

MD

N/A

N/A

Kovesdi; Imre

Rockville

MD

N/A

N/A

US-CL-CURRENT: 435/456; 435/320.1, 435/462, 536/23.1, 536/23.2

ABSTRACT:

The present invention provides methods for site-specific recombination in a cell, as well as vectors which can be employed in such methods. The methods and vectors of the present invention can be used to obtain persistent gene expression in a cell and to modulate gene expression.

One preferred method according to the invention comprises contacting a cell with a vector comprising an origin of replication functional in mammalian cells located between first and second recombining sites located in parallel. Another preferred method comprises, in part, contacting a cell with a vector comprising first and second recombining sites in antiparallel orientations such that the vector is internalized by the cell. In both methods, the cell is further provided with a site-specific recombinase that effects recombination between the first and second recombining sites of the vector.
47 Claims, 7 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 5

43. Document ID: US 5795726 A
Entry 43 of 88

File: USPT

Aug 18, 1998

US-PAT-NO: 5795726
DOCUMENT-IDENTIFIER: US 5795726 A

TITLE: Methods for identifying compounds useful in treating type II diabetes

DATE-ISSUED: August 18, 1998

INVENTOR-INFORMATION:
NAME

CITY

STATE

ZIP CODE

COUNTRY

Glucksmann; M. Alexandra

Somerville

MA

N/A

N/A

US-CL-CURRENT: 435/7.21; 435/4, 435/6, 435/8, 536/23.5

ABSTRACT:

Methods for identifying compounds, which modulate the bioactivity of human hepatic nuclear factor-1 (HNF-1), and which are therefore useful in treating type II diabetes are disclosed.
10 Claims, 5 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 5

44. Document ID: US 5795734 A
Entry 44 of 88

File: USPT

Aug 18, 1998

US-PAT-NO: 5795734
DOCUMENT-IDENTIFIER: US 5795734 A

TITLE: EPH receptor ligands, and uses related thereto

DATE-ISSUED: August 18, 1998

INVENTOR-INFORMATION:
NAME

	CITY	STATE	ZIP CODE	COUNTRY
Flanagan; John G.	Newton	MA	N/A	N/A
Cheng; Hwai-Jong	Boston	MA	N/A	N/A

US-CL-CURRENT: 435/69.1; 435/252.3, 435/320.1, 435/325, 435/7.1, 530/300, 530/350, 536/23.1, 536/23.5

ABSTRACT:

The present invention relates to the discovery of a novel EPH receptor ligand, referred to hereinafter as "Elf-1", which protein has apparently broad involvement in the formation and maintenance of ordered spatial arrangements of differentiated tissues in vertebrates, and can be used to generate and/or maintain an array of different vertebrate tissue both in vitro and in vivo.

26 Claims, 13 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 12

45. Document ID: US 5792833 A
Entry 45 of 88

File: USPT

Aug 11, 1998

US-PAT-NO: 5792833
DOCUMENT-IDENTIFIER: US 5792833 A

TITLE: E2 binding proteins

DATE-ISSUED: August 11, 1998

INVENTOR-INFORMATION:
NAME

	CITY	STATE	ZIP CODE	COUNTRY
Androphy; Elliot J.	Natick	MA	N/A	N/A
Breiding; David E.	Somerville	MA	N/A	N/A

US-CL-CURRENT: 530/350; 530/300

ABSTRACT:

E2-BP polypeptides, nucleic acids encoding E2-BP polypeptides, and uses thereof.

25 Claims, 5 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 5

46. Document ID: US 5789156 A
Entry 46 of 88

File: USPT

Aug 4, 1998

US-PAT-NO: 5789156

DOCUMENT-IDENTIFIER: US 5789156 A

TITLE: Tetracycline-regulated transcriptional inhibitors

DATE-ISSUED: August 4, 1998

INVENTOR-INFORMATION:
NAME

	CITY	STATE	ZIP CODE	COUNTRY
Bujard; Hermann	Heidelberg	N/A	N/A	DEX
Gossen; Manfred	El Cerrito	CA	N/A	N/A

US-CL-CURRENT: 435/6; 435/252.3, 435/320.1, 435/69.1, 435/69.7, 435/810, 536/23.4, 536/23.7, 536/24.1

ABSTRACT:

Nucleic acid molecules and proteins useful for regulating the expression of genes in eukaryotic cells and organisms in a highly controlled manner are disclosed. In the regulatory system of the invention, transcription of a tet operator-linked nucleotide sequence is inhibited by a transcriptional inhibitor fusion protein composed of two polypeptides, a first polypeptide which binds to tet operator sequences either (i) in the absence but not the presence of tetracycline (or an analogue thereof) or (ii) in the presence but not the absence of tetracycline (or an analogue thereof), and a second polypeptide which directly or indirectly inhibits transcription in eukaryotic cells. In one embodiment, the fusion protein comprises a Tet repressor operatively linked to a transcriptional silencer polypeptide. In another embodiment, the fusion protein comprises a mutated Tet repressor operatively linked to a transcriptional silencer polypeptide.

The fusion proteins of the invention are useful for reducing the level of transcription of a tet operator-linked target gene. Moreover, the fusion proteins of the invention can be used in combination with tetracycline-regulated transcriptional activator fusion proteins to allow for precise regulation of the expression of one or multiple target genes. Kits including the components of the regulatory system of the invention are also encompassed by the invention.

49 Claims, 14 Drawing figures

Exemplary Claim Number: 1,2,17,18,19

Number of Drawing Sheets: 12

47. Document ID: US 5780296 A
Entry 47 of 88

File: USPT

Jul 14, 1998

US-PAT-NO: 5780296

DOCUMENT-IDENTIFIER: US 5780296 A

TITLE: Compositions and methods to promote homologous recombination
in eukaryotic cells and
organisms

DATE-ISSUED: July 14, 1998

INVENTOR-INFORMATION:
NAME

CITY

STATE

ZIP CODE

COUNTRY

Holloman, William K.

Yorktown Heights

NY

N/A

N/A

Kmiec, Eric B.

Malvern

PA

N/A

N/A

US-CL-CURRENT: 435/320.1; 536/23.2

ABSTRACT:

The invention concerns genes encoding recombinases that can be used to promote homologous recombination in eukaryotic cells and expression vectors that can be used to transiently express recombinases in target cells. One embodiment of the invention encompasses genetically engineered nucleic acids that encode a non-naturally occurring recombinase that causes a greater rate of recombination than does the naturally occurring recombinase. Recombinases from *Ustilago maydis*, *Saccharomyces cerevisiae* are specifically included in the invention.
26 Claims, 14 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 10

48. Document ID: US 5770384 A
Entry 48 of 88

File: USPT

Jun 23, 1998

US-PAT-NO: 5770384

DOCUMENT-IDENTIFIER: US 5770384 A

TITLE: Method for determining compound interaction with E2 binding
proteins

DATE-ISSUED: June 23, 1998

INVENTOR-INFORMATION:
NAME

CITY

STATE

ZIP CODE

COUNTRY

Androphy, Elliot J.

Natick

MA

N/A

N/A

Breiding, David E.

Somerville

MA

N/A

N/A

US-CL-CURRENT: 435/7.8; 435/5, 435/69.1, 435/69.7, 435/7.1, 435/7.93,
514/2, 530/300, 530/350,
536/23.72

ABSTRACT:

E2-BP polypeptides, nucleic acids encoding E2-BP polypeptides, and uses thereof.

42 Claims, 5 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 5

49. Document ID: US 5763240 A
Entry 49 of 88

File: USPT

Jun 9, 1998

US-PAT-NO: 5763240

DOCUMENT-IDENTIFIER: US 5763240 A

TITLE: In vivo homologous sequence targeting in eukaryotic cells

DATE-ISSUED: June 9, 1998

INVENTOR-INFORMATION:
NAME

CITY

STATE

ZIP CODE

COUNTRY

Zarling, David A.

Menlo Park

CA

N/A

N/A

Sena, Elissa P.

Palo Alto

CA

N/A

N/A

US-CL-CURRENT: 435/463; 435/6, 435/91.1, 435/91.4

ABSTRACT:

The invention relates to methods for targeting an exogenous polynucleotide or exogenous complementary polynucleotide pair to a predetermined endogenous DNA target sequence in a eukaryotic cell by homologous pairing, particularly for altering an endogenous DNA sequence, such as a chromosomal DNA sequence, typically by targeted homologous recombination. In certain embodiments, the invention relates to methods for targeting an exogenous polynucleotide having a linked chemical substituent to a predetermined endogenous DNA sequence in a metabolically active eukaryotic cell, generating a DNA sequence-specific targeting of one or more chemical substituents in an intact nucleus of a metabolically active eukaryotic cell, generally for purposes of altering a predetermined endogenous DNA sequence in the cell. The invention also relates to compositions that contain exogenous targeting polynucleotides,

complementary pairs of
exogenous targeting polynucleotides, chemical substituents of such
polynucleotides, and
recombinase proteins used in the methods of the invention.
47 Claims, 16 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 8

50. Document ID: US 5756671 A
Entry 50 of 88

File: USPT

May 26, 1998

US-PAT-NO: 5756671
DOCUMENT-IDENTIFIER: US 5756671 A

TITLE: CDC37 cell-cycle regulatory protein, and uses related thereto

DATE-ISSUED: May 26, 1998

INVENTOR-INFORMATION:
NAME

	CITY	STATE	ZIP CODE	COUNTRY
Gyuris; Jenő	Winchester	MA	N/A	N/A
Lamphere; Lou	Boston	MA	N/A	N/A
Draetta; Giulio	Milan	N/A	N/A	ITX

US-CL-CURRENT: 530/350; 530/300

ABSTRACT:

The present invention relates to the discovery in mammalian cells, particularly human cells, of a novel CDK-binding protein, referred to herein as "cdc37". As described herein, this protein functions to facilitate activation and accordingly functions in the modulation of cell-cycle progression, and therefore ultimately of cell growth and differentiation. Moreover, binding data indicated that cdc37 may function coordinately with other cell-cycle regulatory proteins, such as of cyclin-dependent kinases (CDKs), src, p53 and erk kinases.
37 Claims, 1 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 1

51. Document ID: US 5744336 A
Entry 51 of 88

File: USPT

Apr 28, 1998

US-PAT-NO: 5744336
DOCUMENT-IDENTIFIER: US 5744336 A

TITLE: DNA constructs for controlled transformation of eukaryotic cells

DATE-ISSUED: April 28, 1998

INVENTOR-INFORMATION:
NAME

	CITY	STATE	ZIP CODE	COUNTRY
Hodges; Thomas K.	West Lafayette	IN	N/A	N/A
Lyznik; Leszek A.	West Lafayette	IN	N/A	N/A

US-CL-CURRENT: 435/320.1; 536/23.1, 536/24.1, 536/24.2

ABSTRACT:

DNA constructs are provided for the creation of transgenic eukaryotic cells. These DNA constructs allow a more precise and effective transformation procedure by enabling the targeting of DNA sequences for insertion into a particular DNA locus, while enabling the removal of any randomly inserted DNA sequences that occur as a by product of known transformation procedures.
15 Claims, 18 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 11

52. Document ID: US 5733733 A
Entry 52 of 88

File: USPT

Mar 31, 1998

US-PAT-NO: 5733733
DOCUMENT-IDENTIFIER: US 5733733 A

TITLE: Methods for the isothermal amplification of nucleic acid molecules

DATE-ISSUED: March 31, 1998

INVENTOR-INFORMATION:
NAME

	CITY	STATE	ZIP CODE	COUNTRY
Auerbach; Jeffrey I.	Rockville	MD	N/A	N/A

US-CL-CURRENT: 435/6; 435/320.1, 435/5, 435/91.1, 435/91.2, 536/23.1, 536/24.3, 536/24.33

ABSTRACT:

Methods for amplifying a nucleic acid molecule which employs a single primer, and in which the amplification is performed under isothermal conditions. The invention also includes kits containing reagents for conducting the method.
26 Claims, 19 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 19

53. Document ID: US 5721118 A
Entry 53 of 88

File: USPT

Feb 24, 1998

US-PAT-NO: 5721118
DOCUMENT-IDENTIFIER: US 5721118 A

TITLE: Mammalian artificial chromosomes and methods of using same

DATE-ISSUED: February 24, 1998

INVENTOR-INFORMATION:
NAME

CITY	STATE	ZIP CODE	COUNTRY
Scheffler, Immo E.	Del Mar	CA	N/A
		N/A	N/A

US-CL-CURRENT: 435/69.1; 435/320.1, 435/325, 435/449, 514/44, 536/23.1, 536/23.5

ABSTRACT:

The present invention provides a mammalian artificial chromosome (MAC), comprising a centromere and a unique cloning site, said MAC containing less than 0.1% of the DNA present in a normal haploid genome of the mammalian cell from which the centromere was obtained. The invention further provides a MAC, wherein the unique cloning site is a nucleic acid sequence encoding a selectable marker. The invention also provides methods of preparing a MAC. In addition, the invention provides methods of stably expressing a selectable marker in a cell, comprising introducing a MAC containing the selectable marker into the cell. The invention also provides a cell containing a MAC expressing an exogenous nucleic acid sequence and a transgenic mammal expressing a selectable marker.
17 Claims, 6 Drawing figures
Exemplary Claim Number: 2,7,17
Number of Drawing Sheets: 3

54. Document ID: US 5681559 A
Entry 54 of 88

File: USPT

Oct 28, 1997

US-PAT-NO: 5681559
DOCUMENT-IDENTIFIER: US 5681559 A

TITLE: Method for producing a highly enriched population of hematopoietic stem cells

DATE-ISSUED: October 28, 1997

INVENTOR-INFORMATION:
NAME

CITY	STATE	ZIP CODE	COUNTRY
DiGiusto, David	Palo Alto	CA	

N/A

N/A

Galy, Anne

Palo Alto

CA

N/A

N/A

US-CL-CURRENT: 424/93.1; 424/93.7, 435/7.2, 435/7.21

ABSTRACT:

The present invention provides a simple and reliable means for isolating populations of hematopoietic cells enriched for stem cell activity on the basis of possession of high CD34 cell surface antigen density ("CD34hi"). CD34.sup.hi cell preparations are useful, for example, for drug discovery efforts, for reconstituting hematopoiesis in an animal lacking a functioning hematopoietic system, and for gene therapies.
17 Claims, 40 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 13

55. Document ID: US 5654168 A
Entry 55 of 88

File: USPT

Aug 5, 1997

US-PAT-NO: 5654168
DOCUMENT-IDENTIFIER: US 5654168 A

TITLE: Tetracycline-inducible transcriptional activator and tetracycline-regulated transcription units

DATE-ISSUED: August 5, 1997

INVENTOR-INFORMATION:
NAME

CITY	STATE	ZIP CODE	COUNTRY
Bujard, Hermann	Heidelberg	N/A	
		N/A	
Gossen, Manfred	Berkeley	CA	DEX
		N/A	N/A

US-CL-CURRENT: 435/69.1; 435/320.1, 536/23.7, 536/24.1

ABSTRACT:

Nucleic acid molecules and proteins useful for regulating the expression of genes in eukaryotic cells and organisms in an inducible manner are disclosed. In the regulatory system of the invention, transcription of a tet operator-linked nucleotide sequence is stimulated by a transcriptional activator fusion protein composed of two polypeptides, a first polypeptide which binds to tet operator sequences in the presence of tetracycline or a tetracycline analogue and a second polypeptide which directly or indirectly activates transcription in eukaryotic cells. In one embodiment, the fusion protein comprises a mutated Tet repressor

operatively linked to a transcriptional activation polypeptide, such as a portion of herpes simplex virus virion protein

16. In the absence of an inducing agent (tetracycline or a tetracycline analogue), transcription of the tet operator-linked nucleotide sequence remains uninduced. In the presence of the inducing agent, transcription of the tet operator-linked nucleotide sequence is stimulated by the transactivator fusion protein of the invention. Novel transcription units which allow for coordinate or independent tetracycline-regulated expression of two or more nucleotide sequences by the transactivator fusion protein of the invention are also disclosed. Kits including the components of the regulatory system of the invention are also encompassed by the invention.

33 Claims, 12 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 10

56. Document ID: US 5650298 A
Entry 56 of 88

File: USPT

Jul 22, 1997

US-PAT-NO: 5650298
DOCUMENT-IDENTIFIER: US 5650298 A

TITLE: Tight control of gene expression in eucaryotic cells by tetracycline-responsive promoters

DATE-ISSUED: July 22, 1997

INVENTOR-INFORMATION:
NAME

	CITY	STATE	ZIP CODE	COUNTRY
Bujard; Hermann	Heidelberg	N/A	N/A	DEX
Gossen; Manfred	Heidelberg	N/A	N/A	DEX
Salfeld; Jochen G.	North Grafton	MA	N/A	N/A
Voss; Jeffrey W.	Framingham	MA	N/A	N/A

US-CL-CURRENT: 435/69.7; 435/320.1, 435/463, 536/23.4, 536/24.1

ABSTRACT:

Transgenic animals carrying two transgenes, the first coding for a transactivator fusion protein comprising a tet repressor and a polypeptide which directly or indirectly activates in eucaryotic cells, and the second comprising a gene operably linked to a minimal promoter operably linked to at least one tet operator sequence, are disclosed. Isolated DNA molecules (e.g., targeting vectors) for integrating a polynucleotide sequence encoding a transactivator

of the invention at a predetermined location within a second target DNA molecule by homologous recombination are also disclosed. Transgenic animals having the DNA molecules of the invention integrated at a predetermined location in a chromosome by homologous recombination are also encompassed by the invention. Methods to regulate the expression of a tet operator linked-gene of interest by administering tetracycline or a tetracycline analogue to an animal of the invention are also disclosed. The regulatory system of the invention allows for conditional inactivation or modulation of expression of a gene of interest in a host cell or animal.

45 Claims, 36 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 32

57. Document ID: US 5635381 A
Entry 57 of 88

File: USPT

Jun 3, 1997

US-PAT-NO: 5635381
DOCUMENT-IDENTIFIER: US 5635381 A

TITLE: Agrobacterium bacteria capable of site-specific recombination

DATE-ISSUED: June 3, 1997

INVENTOR-INFORMATION:
NAME

	CITY	STATE	ZIP CODE	COUNTRY
Hooykaas; Paul J. J.	Leiden	N/A	N/A	NLX
Mozo; Teresa	Berlin	N/A	N/A	DEX

US-CL-CURRENT: 800/294; 435/199, 435/252.2, 435/252.3, 435/320.1, 435/419, 435/477, 435/71.2, 536/23.72

ABSTRACT:

The invention provides Agrobacterium strains capable of producing a cite-specific recombinase capable of effecting site-specific recombination of a first and a second recombination site in Agrobacterium strains, when present therein, comprising a structural DNA sequence encoding said recombinase and a DNA sequence capable of controlling expression in Agrobacterium strains. The invention also provides methods for using the strains to transform plant cells.

20 Claims, 9 Drawing figures
Exemplary Claim Number: 1,16
Number of Drawing Sheets: 9

58. Document ID: US 5631237 A
Entry 58 of 88

File: USPT

May 20, 1997

US-PAT-NO: 5631237
DOCUMENT-IDENTIFIER: US 5631237 A

TITLE: Method for producing in vivo delivery of therapeutic agents via liposomes

DATE-ISSUED: May 20, 1997

INVENTOR-INFORMATION:
NAME

CITY	STATE	ZIP CODE	COUNTRY
Dzau, Victor J.			
Los Altos Hills	CA	94022	N/A
Kaneda, Yasufumi			
Suita-City, Osaka	N/A	N/A	JPX

US-CL-CURRENT: 514/44; 264/4.1, 264/4.3, 264/4.6, 424/417, 424/450, 428/402.2

ABSTRACT:

Methods and compositions are provided for intracellular transfer of a wide variety of agents, by using Sendai virus comprising liposomes having various compositions in the liposome lumen. A preferred method for preparing the liposomes provides for enhanced levels of luminal concentrations, as well as incorporation of high molecular weight molecules. The method comprises fusing liposomes, where one liposome comprises the Sendai virus proteins and the other liposome comprises the luminal composition. The subject methods find particular application with intranuclear transfer of nucleic acids, more particularly with cells of the vasculature.
10 Claims, 27 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 18

59. Document ID: US 5614389 A
Entry 59 of 88

File: USPT

Mar 25, 1997

US-PAT-NO: 5614389
DOCUMENT-IDENTIFIER: US 5614389 A

TITLE: Methods for the isothermal amplification of nucleic acid molecules

DATE-ISSUED: March 25, 1997

INVENTOR-INFORMATION:
NAME

CITY	STATE	ZIP CODE	COUNTRY
Auerbach, Jeffrey I.			
Rockville	MD	N/A	N/A

US-CL-CURRENT: 435/91.2; 435/6, 435/91.1

ABSTRACT:

Methods for amplifying a nucleic acid molecule which employs a single primer, and in which the amplification is performed under isothermal conditions. The invention also includes kits containing reagents for conducting the method.
20 Claims, 19 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 19

60. Document ID: US 5612018 A
Entry 60 of 88

File: USPT

Mar 18, 1997

US-PAT-NO: 5612018
DOCUMENT-IDENTIFIER: US 5612018 A

TITLE: Drug screening and treatment for HIV thymocyte depletion

DATE-ISSUED: March 18, 1997

INVENTOR-INFORMATION:
NAME

CITY	STATE	ZIP CODE	COUNTRY
Bonyhadi, Mark L.			
Belmont	CA	N/A	N/A
Kaneshima, Hideto			
Palo Alto	CA	N/A	N/A
McCune, Joseph M.			
San Francisco	CA	N/A	N/A
Namikawa, Reiko			
Palo Alto	CA	N/A	N/A
Su, Lishan			
Palo Alto	CA	N/A	N/A

US-CL-CURRENT: 424/9.2; 424/553, 424/577, 424/580, 424/582

ABSTRACT:

A method is provided for screening compounds for the ability to suppress thymocyte depletion in thymuses of HIV-infected individuals, particularly enhancing the CD4^{sup}.+ -expressing population as compared to an untreated individual. Particularly, drugs are provided which allow for this result, cyclosporine A being exemplary.
7 Claims, 0 Drawing figures
Exemplary Claim Number: 1

61. Document ID: US 5591609 A
Entry 61 of 88

File: USPT

Jan 7, 1997

US-PAT-NO: 5591609

DOCUMENT-IDENTIFIER: US 5591609 A

TITLE: Methods for the isothermal amplification of nucleic acid molecules

DATE-ISSUED: January 7, 1997

INVENTOR-INFORMATION:
NAME

CITY

STATE

ZIP CODE

COUNTRY

Auerbach; Jeffrey I.

Rockville

MD

N/A

N/A

US-CL-CURRENT: 435/91.2; 435/6, 435/91.1, 435/91.5

ABSTRACT:

Methods for amplifying a nucleic acid molecule which employs a single primer, and in which the amplification is performed under isothermal conditions. The invention also includes kits containing reagents for conducting the method.
15 Claims, 18 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 16

62. Document ID: US 5589362 A
Entry 62 of 88

File: USPT

Dec 31, 1996

US-PAT-NO: 5589362

DOCUMENT-IDENTIFIER: US 5589362 A

TITLE: Tetracycline regulated transcriptional modulators with altered DNA binding specificities

DATE-ISSUED: December 31, 1996

INVENTOR-INFORMATION:
NAME

CITY

STATE

ZIP CODE

COUNTRY

Bujard; Hermann

Heidelberg

N/A

N/A

DEX

Gossen; Manfred

El Cerrito

N/A

N/A

DEX

Hillen; Wolfgang

Erlangen

N/A

N/A

DEX

Helbl; Vera

Fuerth

N/A

N/A

DEX

Schnappinger; Dirk

Bad Driburg

N/A

N/A

DEX

US-CL-CURRENT: 435/69.1; 435/320.1, 435/325, 435/358, 435/455, 536/23.4, 536/24.1

ABSTRACT:

Isolated nucleic acid molecules encoding fusion proteins which regulate transcription in eukaryotic cells are disclosed. The fusion proteins of the invention comprise a Tet repressor having at least one amino acid mutation that confers on the fusion protein an ability to bind a class B tet operator sequence having a nucleotide substitution at position +4 or +6, operatively linked to a polypeptide which regulates transcription in eukaryotic cells. Methods for regulating transcription of a tet operator-linked gene in a cell are also provided. In one embodiment, the method involves introducing into the cell a nucleic acid molecule encoding a fusion protein which regulates transcription, the fusion protein comprising a Tet repressor having at least one amino acid mutation that confers on the fusion protein an ability to bind a class B tet operator sequence having a nucleotide substitution at position +4 or +6, operatively linked to a polypeptide which regulates transcription in eukaryotic cells, and modulating the concentration of a tetracycline, or analogue thereof, in contact with the cell.
20 Claims, 18 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 15

63. Document ID: US 5580734 A
Entry 63 of 88

File: USPT

Dec 3, 1996

US-PAT-NO: 5580734

DOCUMENT-IDENTIFIER: US 5580734 A

TITLE: Method of producing a physical map contiguous DNA sequences

DATE-ISSUED: December 3, 1996

INVENTOR-INFORMATION:
NAME

CITY

STATE

ZIP CODE

COUNTRY

Treco; Douglas A.

Arlington

MA

N/A

N/A

Miller; Allan M.

Medford

MA

N/A

N/A

US-CL-CURRENT: 435/6; 435/489

ABSTRACT:

Materials and methods for homologous-recombination screening of DNA libraries constructed in a

eukaryotic host and methods for homologous-recombination chromosome walking for isolating overlapping DNA sequences for building an extended physical map of a chromosomal region.
4 Claims, 17 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 17

64. Document ID: US 5571688 A
Entry 64 of 88

File: USPT

Nov 5, 1996

US-PAT-NO: 5571688
DOCUMENT-IDENTIFIER: US 5571688 A

TITLE: Method of detecting gene expression

DATE-ISSUED: November 5, 1996

INVENTOR-INFORMATION:
NAME

	CITY	STATE	ZIP CODE	COUNTRY
Mekalanos; John J.	Cambridge	MA	02138	N/A
Camilli; Andrew	Chestnut Hill	MA	02167	N/A

US-CL-CURRENT: 435/29; 435/34, 435/6

ABSTRACT:

A reporter system relating to in vivo expression technology was devised to aid in the identification and study of genes that display temporal or spatial patterns of expression during infection of host tissues. The method of this invention comprises constructing a strain or pool of strains of a microorganism which contains an artificial cointegrate comprising a reporter gene flanked by direct repeats of sequences to which a resolvase enzyme binds, thus catalyzing excision of the reporter gene, and further contains a coding sequence under the control of a promoter sequence which encodes transcripts, the expression of which are easily monitored in vitro and which result in a permanent genetic change, excision of the reporter gene, that is heritable and easily detectable subsequent to induction of the synthetic operon.

16 Claims, 17 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 15

65. Document ID: US 5527695 A
Entry 65 of 88

File: USPT

Jun 18, 1996

US-PAT-NO: 5527695
DOCUMENT-IDENTIFIER: US 5527695 A

TITLE: Controlled modification of eukaryotic genomes

DATE-ISSUED: June 18, 1996

INVENTOR-INFORMATION:
NAME

	CITY	STATE	ZIP CODE	COUNTRY
Hodges; Thomas K.	West Lafayette	IN	N/A	N/A
Lyznik; Leszek A.	West Lafayette	IN	N/A	N/A

US-CL-CURRENT: 800/291; 435/320.1

ABSTRACT:

DNA constructs are provided for the creation of transgenic eukaryotic cells. These DNA constructs allow a more precise and effective transformation procedure by enabling the targeting of DNA sequences for insertion into a particular DNA locus, while enabling the removal of any randomly inserted DNA sequences that occur as a by product of known transformation procedures.
6 Claims, 13 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 11

66. Document ID: US 5512452 A
Entry 66 of 88

File: USPT

Apr 30, 1996

US-PAT-NO: 5512452
DOCUMENT-IDENTIFIER: US 5512452 A

TITLE: Selection of bacterial genes induced in host tissues

DATE-ISSUED: April 30, 1996

INVENTOR-INFORMATION:
NAME

	CITY	STATE	ZIP CODE	COUNTRY
Mekalanos; John J.	Cambridge	MA	N/A	N/A
Camilli; Andrew	Chestnut Hill	MA	N/A	N/A

US-CL-CURRENT: 435/25; 435/6

ABSTRACT:

A reporter system relating to in vivo expression technology was devised to aid in the identification and study of genes that display temporal or spatial patterns of

expression during infection of host tissues. The method of this invention comprises integrating a site-specific DNA recombinase expression vector, and a reporter gene that is permanently removable by the recombinase, by way of homologous recombination into a microorganism's chromosome and inducing the expression of a synthetic operon which encodes transcripts, the expression of which are easily monitored in vitro and which result in a permanent genetic change, excision of the reporter gene, that is heritable and easily detectable subsequent to induction of the synthetic operon.
 16 Claims, 13 Drawing figures
 Exemplary Claim Number: 1
 Number of Drawing Sheets: 11

67. Document ID: US 5434066 A
 Entry 67 of 88

File: USPT

Jul 18, 1995

US-PAT-NO: 5434066

DOCUMENT-IDENTIFIER: US 5434066 A

TITLE: Modulation of CRE recombinase in the in vivo cloning of DNA

DATE-ISSUED: July 18, 1995

INVENTOR-INFORMATION:
 NAME

CITY

STATE

ZIP CODE

COUNTRY

Bebee; Robert L.

Gaithersburg

MD

N/A

N/A

Hartley; James L.

Frederick

MD

N/A

N/A

US-CL-CURRENT: 435/475; 435/252.3, 435/252.33, 435/476

ABSTRACT:

Methods and recombinant vectors suitable for accomplishing the in vivo alteration of a nucleic acid molecule are disclosed. The invention in particular discloses the use of recombinases such as Cre to accomplish in vivo recombination.
 7 Claims, 0 Drawing figures
 Exemplary Claim Number: 1

68. Document ID: US 5354668 A
 Entry 68 of 88

File: USPT

Oct 11, 1994

US-PAT-NO: 5354668

DOCUMENT-IDENTIFIER: US 5354668 A

TITLE: Methods for the isothermal amplification of nucleic acid molecules

DATE-ISSUED: October 11, 1994

INVENTOR-INFORMATION:

NAME

CITY

STATE

ZIP CODE

COUNTRY

Auerbach; Jeffrey I.

Rockville

MD

20850

N/A

US-CL-CURRENT: 435/91.1; 435/6

ABSTRACT:

Methods for amplifying a nucleic acid molecule which employs a single primer, and in which the amplification is performed under isothermal conditions. The invention also includes kits containing reagents for conducting the method.
 22 Claims, 14 Drawing figures
 Exemplary Claim Number: 20
 Number of Drawing Sheets: 14

69. Document ID: US 5102797 A
 Entry 69 of 88

File: USPT

Apr 7, 1992

US-PAT-NO: 5102797

DOCUMENT-IDENTIFIER: US 5102797 A

TITLE: Introduction of heterologous genes into bacteria using transposon flanked expression cassette and a binary vector system

DATE-ISSUED: April 7, 1992

INVENTOR-INFORMATION:
 NAME

CITY

STATE

ZIP CODE

COUNTRY

Tucker; William T.

Oakland

CA

N/A

N/A

Gutterson; Neal I.

Oakland

CA

N/A

N/A

US-CL-CURRENT: 435/473; 435/320.1

ABSTRACT:

This invention relates to a new method for inserting heterologous genes into the genome of a bacteria using a combined plasmid. The combined plasmid provides a cis complementation of transposase genes and transposable elements. The method involves the homologous recombination of a carrier plasmid and a functions plasmid to form the combined plasmid. The carrier plasmid contains a transposable element which flanks a generic expression cassette. The functions plasmid comprises transposase genes which complement the transposable element on the carrier plasmid. The combined plasmid is then transferred to a recipient and the recipient is

monitored for
integration of the generic expression cassette into the genome. The
combined plasmid is
preferably created by an in vivo homologous recombination of the carrier
and functions plasmids.

17 Claims, 4 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 5

70. Document ID: US 4997757 A
Entry 70 of 88

File: USPT

Mar 5, 1991

US-PAT-NO: 4997757
DOCUMENT-IDENTIFIER: US 4997757 A

TITLE: Process for detecting potential carcinogens

DATE-ISSUED: March 5, 1991

INVENTOR-INFORMATION:
NAME

CITY

STATE

ZIP CODE

COUNTRY

Schiestl, Robert H.

Rochester

NY

N/A

N/A

US-CL-CURRENT: 435/6; 435/29

ABSTRACT:

There is provided a process for screening an agent in order to determine
whether such agent
increases the frequency of genome rearrangement in living matter.

In the first step of this process, there is provided a viable species of
Saccharomyces cerevisiae
yeast which comprises repeated genetic elements in its haploid genome.
These repeated genetic
elements are selected from the group consisting of functional and
non-functional genetic
elements; and these elements are sufficiently homologous so that, under
ambient conditions, they
recombine with each other and give rise to an indentifiable genome
rearrangement which is a
deletion.

In the second step of this process, the viable species of yeast is exposed to
the agent to be
tested. Thereafter, it is plated onto a growth medium which, after the
exposed yeast species
grows upon it, facilitates the identification of those yeast which have
undergone said genome
rearrangement.

In the last step of the process, the extent to which the exposed species of
yeast has undergone
genome rearrangement is determined.

Also disclosed is a the viable yeast strain used in said process, the plasmid
used to construct
said strain, and a process for constructing said strain.

20 Claims, 10 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 7

71. Document ID: US 4959317 A
Entry 71 of 88

File: USPT

Sep 25, 1990

US-PAT-NO: 4959317
DOCUMENT-IDENTIFIER: US 4959317 A

TITLE: Site-specific recombination of DNA in eukaryotic cells

DATE-ISSUED: September 25, 1990

INVENTOR-INFORMATION:
NAME

CITY

STATE

ZIP CODE

COUNTRY

Sauer, Brian L.

Greenville

DE

N/A

N/A

US-CL-CURRENT: 435/462; 435/254.2, 435/254.21, 435/320.1, 435/477,
435/69.1, 435/91.1, 435/91.41

ABSTRACT:

A method for producing site-specific recombination of DNA in eukaryotic
cells at regions
designated lox sites is disclosed.
40 Claims, 11 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 9

72. Document ID: JP 11225785 A
Entry 72 of 88

File: JPAB

Aug 24, 1999

PUB-NO: JP411225785A
DOCUMENT-IDENTIFIER: JP 11225785 A
TITLE: OPTIMIZATION OF CELL FOR ENDOGENOUS GENE
ACTIVATION

PUBN-DATE: August 24, 1999

INVENTOR-INFORMATION:
NAME

COUNTRY

HONOLD, KONRAD

N/A

HOLTSCHKE, THOMAS

N/A

STERN, ANNE

N/A

INT-CL (IPC): C12 N 15/09; C12 N 5/10; C12 Q 1/68

ABSTRACT:

PROBLEM TO BE SOLVED: To optimize the expression of a nucleic acid
in cells by transfecting cells
with a vector comprising a heteroexpression control sequence or the like,
positive selection
marker gene, site-specific recombinase target sequence and sequence
capable of homologous
recombination, followed by culturing the resultant cells.

SOLUTION: The expression of a nucleic acid sequence endogenous in
eukaryocytes is optimized by

the following procedure: cells are transfected with a 1st vector comprising a 1st heteroexpression control sequence and a sequence of a 1st amplification gene or the like, positive selection marker gene, at least two target sequences of a site-specific recombinase, adjacent to the above sequences, and such a DNA sequence as to be adjacent to the above sequences and homologous with the nucleic acid portion in the genome of the cells so as to be capable of homologous recombination; the resulting transfected cells are cultured under such conditions as to cause the homologous recombination of the above vector, and the resulting cells are isolated.

COPYRIGHT: (C)1999,JPO

73. Document ID: JP 11225785 A
Entry 73 of 88

File: JPAB

Aug 24, 1999

PUB-NO: JP411225785A
DOCUMENT-IDENTIFIER: JP 11225785 A
TITLE: OPTIMIZATION OF CELL FOR ENDOGENOUS GENE ACTIVATION

PUBN-DATE: August 24, 1999

INVENTOR-INFORMATION:
NAME

COUNTRY
HONOLD, KONRAD
N/A
HOLTSCHKE, THOMAS
N/A
STERN, ANNE
N/A

INT-CL (IPC): C12 N 15/09; C12 N 5/10; C12 Q 1/68

ABSTRACT:

PROBLEM TO BE SOLVED: To optimize the expression of a nucleic acid in cells by transfecting cells with a vector comprising a heteroexpression control sequence or the like, positive selection marker gene, site-specific recombinase target sequence and sequence capable of homologous recombination, followed by culturing the resultant cells.

SOLUTION: The expression of a nucleic acid sequence endogenous in eukaryocytes is optimized by the following procedure: cells are transfected with a 1st vector comprising a 1st heteroexpression control sequence and a sequence of a 1st amplification gene or the like, positive selection marker gene, at least two target sequences of a site-specific recombinase, adjacent to the above sequences, and such a DNA sequence as to be adjacent to the above sequences and homologous with the nucleic acid portion in the genome of the cells so as to be capable of homologous recombination; the resulting transfected cells are cultured under such conditions as to cause the homologous recombination of the above vector, and the resulting cells are isolated.

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74. Document ID: US 5780296 A

Entry 74 of 88

File: EPAB

Jul 14, 1998

PUB-NO: US005780296A
DOCUMENT-IDENTIFIER: US 5780296 A
TITLE: Compositions and methods to promote homologous recombination in eukaryotic cells and organisms
PUBN-DATE: July 14, 1998

INVENTOR-INFORMATION:
NAME

COUNTRY
HOLLOMAN, WILLIAM K
US
KMEIC, ERIC B
US

INT-CL (IPC): C12 N 15/63

EUR-CL (EPC): C12N009/00

ABSTRACT:

The invention concerns genes encoding recombinases that can be used to promote homologous recombination in eukaryotic cells and expression vectors that can be used to transiently express recombinases in target cells. One embodiment of the invention encompasses genetically engineered nucleic acids that encode a non-naturally occurring recombinase that causes a greater rate of recombination than does the naturally occurring recombinase. Recombinases from *Ustilago maydis*, *Saccharomyces cerevisiae* are specifically included in the invention.

75. Document ID: US 5763240 A
Entry 75 of 88

File: EPAB

Jun 9, 1998

PUB-NO: US005763240A
DOCUMENT-IDENTIFIER: US 5763240 A
TITLE: In vivo homologous sequence targeting in eukaryotic cells
PUBN-DATE: June 9, 1998

INVENTOR-INFORMATION:
NAME

COUNTRY
ZARLING, DAVID A
US
SENA, ELISSA P
US

INT-CL (IPC): C12 N 15/64; C12 N 15/90; C12 Q 1/68; C12 P 19/34

EUR-CL (EPC): C12N015/90

ABSTRACT:

The invention relates to methods for targeting an exogenous polynucleotide or exogenous complementary polynucleotide pair to a predetermined endogenous DNA target sequence in a eukaryotic cell by homologous pairing, particularly for altering an endogenous DNA sequence, such as a chromosomal DNA sequence, typically by targeted homologous recombination. In certain embodiments, the invention relates to methods for targeting an exogenous

polynucleotide having a
linked chemical substituent to a predetermined endogenous DNA sequence
in a metabolically active
eukaryotic cell, generating a DNA sequence-specific targeting of one or
more chemical
substituents in an intact nucleus of a metabolically active eukaryotic cell,
generally for
purposes of altering a predetermined endogenous DNA sequence in the cell.
The invention also
relates to compositions that contain exogenous targeting polynucleotides,
complementary pairs of
exogenous targeting polynucleotides, chemical substituents of such
polynucleotides, and
recombinase proteins used in the methods of the invention.

76. Document ID: WO 9811214 A1
Entry 76 of 88

File: EPAB

Mar 19, 1998

PUB-NO: WO009811214A1
DOCUMENT-IDENTIFIER: WO 9811214 A1
TITLE: MAMMALIAN AND HUMAN REC2
PUBN-DATE: March 19, 1998

INVENTOR-INFORMATION:
NAME

COUNTRY
HOLLOMAN, WILLIAM K
N/A
RICE, MICHAEL C
N/A
SMITH, SHERYL T
N/A
SHU, ZHIGANG
N/A
KMIEC, ERIC B
N/A

INT-CL (IPC): C12 N 15/12; C12 N 15/87; C12 P 19/34

EUR-CL (EPC): C12N009/00

ABSTRACT:

The invention concerns mammalian recombinase genes (REC2) and their
promoters. Over expression of
REC2 in a cell is found to facilitate homologous recombination, particularly
homologous
recombination using a DNA/RNA chimeric oligonucleotide and to sensitize
a cell to the apoptotic
effects of irradiation. The REC2 promoter, in combination with a strong
enhancer, e.g., a SV40
enhancer, was found to be a strong promoter following irradiation of the
cells. A radiation
inducible promoter can be used to sensitize a cell to radiation treatment by
operably linking
the radiation inducible promoter to a gene whose expression converts a
prodrug to a drug such as
a herpes thymidine kinase gene.

77. Document ID: WO 9630498 A1
Entry 77 of 88

File: EPAB

Oct 3, 1996

PUB-NO: WO009630498A1
DOCUMENT-IDENTIFIER: WO 9630498 A1

TITLE: PRODUCTION OF ANTIBODIES USING CRE-MEDIATED
SITE-SPECIFIC RECOMBINATION
PUBN-DATE: October 3, 1996

INVENTOR-INFORMATION:

NAME
COUNTRY
JAKOBOVITS, AYA
N/A
ZSEBO, KRISZTINA M
N/A

INT-CL (IPC): C12 N 5/00; C12 N 5/06; C12 N 5/16; C12 N 15/00; C12
N 15/06; C12 N 15/09; C12 N
15/13

EUR-CL (EPC): A01K067/027 ; C07K016/00 , C12N015/90

ABSTRACT:

A method to produce a cell expressing an antibody from a genomic
sequence of a cell which has a
modified immunoglobulin locus is disclosed. The method takes advantage
of Cre-mediated
site-specific recombination and homologous recombination. The method
involves first introducing a
lox site into an immunoglobulin locus and then using the lox site as a target
for introduction of
gene modifications via Cre-mediated in vivo recombination.

78. Document ID: WO 9622364 A1
Entry 78 of 88

File: EPAB

Jul 25, 1996

PUB-NO: WO009622364A1
DOCUMENT-IDENTIFIER: WO 9622364 A1
TITLE: COMPOSITIONS AND METHODS TO PROMOTE
HOMOLOGOUS RECOMBINATION IN EUKARYOTIC CELLS AND
ORGANISMS
PUBN-DATE: July 25, 1996

INVENTOR-INFORMATION:

NAME
COUNTRY
HOLLOMAN, WILLIAM K
N/A
KMIEC, ERIC B
N/A

INT-CL (IPC): C12 N 9/00; C12 N 9/22

EUR-CL (EPC): C12N009/00

ABSTRACT:

The invention concerns genes encoding recombinases that can be used to
promote homologous
recombination in eukaryotic cells. The application teaches methods by
which a recombinase of one
species can be used to isolate a homologous recombinase of a different
species and methods to
identify the isolated homologs. Recombinases from *Ustilago maydis* and
Saccharomyces cerevisiae
are specifically included in the invention. The invention encompasses the
method of producing an
isolated recombinase protein in a prokaryotic cell and recovering the
product in an active form.
The invention also encompasses a genetically engineered gene which
encodes a non-naturally

occurring recombinase that causes a greater rate of recombination than does the naturally occurring recombinase. The invention further encompasses the use of recombinase proteins and of recombinase genes to promote homologous recombination, including recombination between a host cell genome and a chimeric oligonucleotide, i.e., an oligonucleotide having both RNA and DNA bases.

79. Document ID: US 5512452 A
Entry 79 of 88

File: EPAB

Apr 30, 1996

PUB-NO: US005512452A
DOCUMENT-IDENTIFIER: US 5512452 A
TITLE: Selection of bacterial genes induced in host tissues
PUBN-DATE: April 30, 1996

INVENTOR-INFORMATION:
NAME

COUNTRY
MEKALANOS, JOHN J
US
CAMILLI, ANDREW
US

INT-CL (IPC): C12 Q 1/02; C12 N 15/00

EUR-CL (EPC): C07K014/255 ; C12N015/10 , C12N015/52 ,
C12N015/62 , C12N015/90 , C12Q001/68

ABSTRACT:

A reporter system relating to in vivo expression technology was devised to aid in the identification and study of genes that display temporal or spatial patterns of expression during infection of host tissues. The method of this invention comprises integrating a site-specific DNA recombinase expression vector, and a reporter gene that is permanently removable by the recombinase, by way of homologous recombination into a microorganism's chromosome and inducing the expression of a synthetic operon which encodes transcripts, the expression of which are easily monitored in vitro and which result in a permanent genetic change, excision of the reporter gene, that is heritable and easily detectable subsequent to induction of the synthetic operon.

80. Document ID: WO 9322443 A1
Entry 80 of 88

File: EPAB

Nov 11, 1993

PUB-NO: WO009322443A1
DOCUMENT-IDENTIFIER: WO 9322443 A1
TITLE: IN VIVO HOMOLOGOUS SEQUENCE TARGETING IN
EUKARYOTIC CELLS
PUBN-DATE: November 11, 1993

INVENTOR-INFORMATION:
NAME

COUNTRY

ZARLING, DAVID A
N/A
SENA, ELISSA P
N/A

INT-CL (IPC): C12N 15/90; C12N 5/10; C12Q 1/68; G01N 33/68; A61K 48/00; A01K 67/027

EUR-CL (EPC): C12N015/90 ; C07K014/47 , C07K014/82

ABSTRACT:

The invention relates to methods for targeting an exogenous polynucleotide or exogenous complementary polynucleotide pair to a predetermined endogenous DNA target sequence in a eukaryotic cell by homologous pairing, particularly for altering an endogenous DNA sequence, such as a chromosomal DNA sequence, typically by targeted homologous recombination. In certain embodiments, the invention relates to methods for targeting an exogenous polynucleotide having a linked chemical substituent to a predetermined endogenous DNA sequence in a metabolically active eukaryotic cell, generating a DNA sequence-specific targeting of one or more chemical substituents in an intact nucleus of a metabolically active eukaryotic cell, generally for purposes of altering a predetermined endogenous DNA sequence in the cell. The invention also relates to compositions that contain exogenous targeting polynucleotides, complementary pairs of exogenous targeting polynucleotides, chemical substituents of such polynucleotides, and recombinase proteins used in the methods of the invention.

81. Document ID: WO 9937755 A2
Entry 81 of 88

File: DWPI

Jul 29, 1999

DERWENT-ACC-NO: 1999-458689
DERWENT-WEEK: 199938
COPYRIGHT 1999 DERWENT INFORMATION LTD
TITLE: New compositions and methods for targeting sequence
modifications in related family genes
INVENTOR: LEHMAN, C W; PATI, S ; ZARLING, D ; ZENG, H

PRIORITY-DATA:
1997US-0070734

December 11, 1997

PATENT-FAMILY:
PUB-NO

PUB-DATE

LANGUAGE

PAGES

MAIN-IPC

WO 9937755 A2

July 29, 1999

E

047

C12N015/00

INT-CL (IPC): C12 N 15/00

ABSTRACTED-PUB-NO: WO 9937755A
BASIC-ABSTRACT:

NOVELTY - A composition is new comprising at least one recombinase

and at least two single-stranded targeting polynucleotides (I) which are substantially complementary to each other and each having a consensus homology clamp for a gene family i.e. a homology motif tag (HMT).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method (A) for targeting a sequence modification in at least one member of a consensus family of genes in a cell by homologous recombination. The method involves introducing into at least one cell at least one recombinase and (I);

(2) a method (B) of making a non-human organism with a targeted sequence modification in at least one member of a gene family by introducing into a cell at least one recombinase and (I). The animal formed has at least one modification in at least one member of a consensus family of genes;

(3) a method (C) of isolating a member of a gene family comprising a protein consensus sequence. The method involves:

(a) adding the recombinase and (I) to a complex mixture of nucleic acids where the targeting polynucleotides comprise a purification tag; and

(b) isolating the member using the purification tag; and

(4) a non-human organism containing a sequence modification in an endogenous consensus functional domain of a gene member of a gene family.

USE - The composition is useful in kit form which include the composition as libraries or pools of degenerate cDNA probes along with other reagents such as recombinase etc. The methods and compositions are used for inactivation of a gene family gene i.e. exogenous targeting polynucleotides can be used to inactivate, decrease or alter the biological activity of one or more genes in a cell (or transgenic nonhuman animal or plant). This is useful in the generation of animal models of disease, or in the elucidation of gene function and activity. Alternatively, the biological activity of the wild-type gene may be either decreased or the wild-type activity altered to mimic disease states. This includes genetic manipulation of non-coding gene sequences that affect the transcription of genes, including promoter, repressors, enhancers and transcriptional activating sequences.

The compositions are useful in identifying new members of gene families which may be useful in functional genomic studies as well as in identification of new drug targets. HMTs used in homologous recombination methods can generate animals that have a wide variety of mutations in a wide variety of related genes, potentially resulting in a wide variety of phenotypes including those related to disease states. This may also be done on a cellular level to identify genes involved in cellular phenotypes i.e. target identification.

ADVANTAGE - This invention provides compositions and methods for the evaluation and characterization of individual and sets of genes in disease states.

Traditionally, exogenous sequences transferred into eukaryotic cells underwent homologous recombination with homologous endogenous sequences only at very low frequencies. Hence they were recombined inefficiently and large numbers of cells were needed to be

transfected, selected and screened in order to generate a correctly targeted homologous recombinant. Several proteins or purified extracts having the property of promoting homologous recombination (recombinase activity) have recently been identified and the frequency of homologous recombination is enhanced by the presence of these recombinase activities. Such recent advances have resulted in techniques allowing enhanced homologous recombination (EHR).

Relaxing the amount of sequence identity needed for homologous recombination allows greater flexibility to target related genes for creating transgenic animals and cells containing modifications in gene family consensus sequences.

82. Document ID: US 5948653 A, WO 9842727 A1, AU 9865620 A
Entry 82 of 88

File: DWPI

Sep 7, 1999

DERWENT-ACC-NO: 1998-542274

DERWENT-WEEK: 199943

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TITLE: Modification of target polynucleotide sequences - by homologous recombination using recombinase and at least 2 single stranded polynucleotides complementary to each other, used for, e.g. correcting diseased alleles in cystic fibrosis
INVENTOR: PATI, S; ZARLING, D A

PRIORITY-DATA:

1997US-0910367

August 13, 1997

1997US-0041173

March 21, 1997

PATENT-FAMILY:

PUB-NO

PUB-DATE

LANGUAGE

PAGES

MAIN-IPC

US 5948653 A

September 7, 1999

N/A

000

C07H021/04

WO 9842727 A1

October 1, 1998

E

136

C07H021/04

AU 9865620 A

October 20, 1998

N/A

000

C07H021/04

INT-CL (IPC): C07 H 21/04; C07 K 14/00; C12 N 15/00; C12 P 19/34

ABSTRACTED-PUB-NO: US 5948653A

BASIC-ABSTRACT:

The following are claimed: (1) preparation of a targeted sequence modification (TSM) in a preselected target DNA sequence in a eukaryotic zygote by homologous recombination, comprising introducing into at least 1 eukaryotic zygote at least 1 recombinase and at least 2 single-stranded (ss) targeting polynucleotides (PNs) that are complementary

to each other, and
 each having a homology clamp (HC) corresponding to or is complementary to a preselected target
 DNA sequence; (2) preparation of TSM in a preselected target DNA sequence in a cell by homologous recombination which contains an insertion, carried out as in (1), but where PNs also each have an internal HC; (3) a method for targeting and altering, by homologous recombination, a pre-selected target NA sequence in an extrachromosomal sequence (ExS) of a prokaryotic cell, comprising: (a) adding to the extrachromosomal sequence materials as in (1); (b) removing the recombinase, and
 (c) introducing the altered element into a prokaryotic cell; (4) a method of generating a pool of variant NA sequences of a pre-selected target NA sequence in ExS, comprising adding to ExS at least 1 recombinase and pairs of ss targeting PNS which are complementary to each other and each comprising HC corresponding to or being complementary to a preselected target NA sequence, the pairs comprising a library of mismatches between the targeting PN and the target NA sequence, to form a library of altered ExS's; (5) a method of generating a cellular library comprising variant NA sequences of a pre-selected target NA sequence, comprising introducing into a population of target cells materials as in (4), and (6) a method similar to (5) comprising: (a) adding to ExS materials as in (4), to form altered ExS's; (b) as in (3b), and (c) introducing the altered sequences into a population of a target cells to form the library of variant NA sequences.

USE - The method of (1) may be used for targeting and altering, by homologous recombination, a pre-selected target nucleic acid (NA) sequence (claimed). The methods can provide for the efficient and specific modification of targeted PNs. The methods can be used, e.g. to target chemical substituents in a sequence-specific manner in vivo, to correct or to generate genetic mutations in endogenous DNA sequences by homologous recombination and/or gene conversion, to produce homologously targeted transgenic organisms, including animals and plants at high efficiency, and in other application, e.g. targeted drug delivery, based on in vivo homologous pairing. The methods can be used for correcting disease alleles involved in producing human genetic diseases, such as inherited genetic diseases (e.g. cystic fibrosis) and neoplasia (e.g. neoplasms induced by somatic mutation of an oncogene or tumour suppressor gene, such as p53) or acquired diseases, particularly parasitic or viral diseases, such as human hepatitis B virus (HBV) infection.

ABSTRACTED-PUB-NO:

WO 9842727A EQUIVALENT-ABSTRACTS:

The following are claimed: (1) preparation of a targeted sequence modification (TSM) in a preselected target DNA sequence in a eukaryotic zygote by homologous recombination, comprising introducing into at least 1 eukaryotic zygote at least 1 recombinase and at least 2 single-stranded (ss) targeting polynucleotides (PNs) that are complementary to each other, and each having a homology clamp (HC) corresponding to or is complementary to a preselected target DNA sequence; (2) preparation of TSM in a preselected target DNA sequence in a cell by homologous recombination which contains an insertion, carried out as in (1), but where PNs also each have an internal HC; (3) a method for targeting and altering, by homologous recombination, a pre-selected target NA sequence in an extrachromosomal sequence (ExS) of a

prokaryotic cell, comprising: (a) adding to the extrachromosomal sequence materials as in (1); (b) removing the recombinase, and
 (c) introducing the altered element into a prokaryotic cell; (4) a method of generating a pool of variant NA sequences of a pre-selected target NA sequence in ExS, comprising adding to ExS at least 1 recombinase and pairs of ss targeting PNS which are complementary to each other and each comprising HC corresponding to or being complementary to a preselected target NA sequence, the pairs comprising a library of mismatches between the targeting PN and the target NA sequence, to form a library of altered ExS's; (5) a method of generating a cellular library comprising variant NA sequences of a pre-selected target NA sequence, comprising introducing into a population of target cells materials as in (4), and (6) a method similar to (5) comprising: (a) adding to ExS materials as in (4), to form altered ExS's; (b) as in (3b), and (c) introducing the altered sequences into a population of a target cells to form the library of variant NA sequences.

USE - The method of (1) may be used for targeting and altering, by homologous recombination, a pre-selected target nucleic acid (NA) sequence (claimed). The methods can provide for the efficient and specific modification of targeted PNs. The methods can be used, e.g. to target chemical substituents in a sequence-specific manner in vivo, to correct or to generate genetic mutations in endogenous DNA sequences by homologous recombination and/or gene conversion, to produce homologously targeted transgenic organisms, including animals and plants at high efficiency, and in other application, e.g. targeted drug delivery, based on in vivo homologous pairing. The methods can be used for correcting disease alleles involved in producing human genetic diseases, such as inherited genetic diseases (e.g. cystic fibrosis) and neoplasia (e.g. neoplasms induced by somatic mutation of an oncogene or tumour suppressor gene, such as p53) or acquired diseases, particularly parasitic or viral diseases, such as human hepatitis B virus (HBV) infection.

83. Document ID: CA 2216596 A, AU 9739226 A, EP 841402 A2, JP 10155485 A, AU 694393 B, AU 9868048 A
 Entry 83 of 88

File: DWPI

Mar 26, 1998

DERWENT-ACC-NO: 1998-251707
 DERWENT-WEEK: 199927
 COPYRIGHT 1999 DERWENT INFORMATION LTD
 TITLE: Shuttle vector for transforming plants with large DNA fragments - contains T-DNA border sequences and Ri ori origin of replication
 INVENTOR: KAWASAKI, S

PRIORITY-DATA:
 1996JP-0255184

September 26, 1996

PATENT-FAMILY:
 PUB-NO

PUB-DATE

LANGUAGE

PAGES

MAIN-IPC

CA 2216596 A

March 26, 1998 N/A 000 C12N015/84

AU 9739226 A

April 2, 1998 N/A 041 C12N015/03

EP 841402 A2

May 13, 1998 E 000 C12N015/82

JP 10155485 A

June 16, 1998 N/A 050 C12N015/09

AU 694393 B

July 16, 1998 N/A 000 C12N015/03

AU 9868048 A

July 30, 1998 N/A 000 C12N015/03

INT-CL (IPC): A01 H 5/00; C07 K 14/415; C12 N 1/20; C12 N 1/21; C12 N 5/10; C12 N 15/01; C12 N 15/03; C12 N 15/09; C12 N 15/10; C12 N 15/63; C12 N 15/68; C12 N 15/82; C12 N 15/84; C12 Q 1/68; C12 N 15/09; C12 R 1/91; C12 N 5/10; C12 R 1/91

ABSTRACTED-PUB-NO: AU 9739226A
BASIC-ABSTRACT:

High-capacity binary shuttle vector comprising T-DNA region and only Ri ori, or Ri ori and RK2 ori as the replication origin is new. Also claimed are: (i) a binary vector comprising a lox site in T-DNA region, a par C gene and an Ri ori replication origin, where the vector is capable of integrating a clone plasmid of a circular genome library with lox site by cre enzyme in an E. coli or Agrobacterium host; (ii) a binary vector for plant transformation comprising a multi-cloning site sandwiched by with a promoter and a terminator for plants in a T-DNA region and an Ri ori as replication origin; (iii) a genomic library having the ability to transform plants, preferably monocotyledonous plants; (iv) a genomic library having the ability to transform plants, where the library comprises a high-capacity binary shuttle vector as above; (v) a complementation method for assessing the function of genes in a genome fragment inserted into a clone of the genomic library of (iv), comprising i introducing the vector into an Agrobacterium cell and transferring the Agrobacterium into a plant; (vi) a complementation method for assessing the function of genes in a genome fragment inserted into a clone of a genomic library comprising integrating a plasmid clone constituting a library and a binary vector as above, where the library is constructed using a circular vector having a lox site and has E. coli as a host, introducing the integrated vector into an Agrobacterium cell and transferring the cell into a plant; (vii) a gene obtained with the method of (v) and (vi); (viii) a method for screening a useful gene comprising using a high-capacity binary shuttle vector as above; (ix) a transformed plant made using a binary vector as above or by introduction of the genes obtained in (vii); (x)

a method for producing a high-efficiency Agrobacterium with recA- to maintain stably the binary vector with large insert comprising generating high transformation efficiency strains by the site-directed mutation on recA gene of said strain to transform to a recA- strain, introducing a homologous recombination to the strains with recA+ genes, between the transformed recA- vector and recA+ gene in the cell, selecting the recombinant by making a replica of the plate on which the strains are spread and irradiating the plate to screen a clone which can not grow under UV irradiation; and (xi) a high transformation efficiency Agrobacterium strain with recA+-, where the strain can maintain stably the high capacity binary vector with large insert.

USE - The methods and products are used to introduce genomic fragments of 10 kb or more into plants, including agriculturally important monocotyledonous plants.

ADVANTAGE - The processes are an alternative to forced introduction methods such as use of gene guns for intact cells or electroporation or polyethylene glycol methods for protoplasts. The former requires expensive facilities to process a small number of samples at a time, and the latter suffers from the drawback that regeneration from protoplasts to normal cells is difficult.

84. Document ID: KR 98703366 A, WO 9630498 A1, AU 9655310 A, EP 817835 A1, JP 11503015 W, AU 707813 B
Entry 84 of 88

File: DWPI

Oct 15, 1998

DERWENT-ACC-NO: 1996-485448
DERWENT-WEEK: 199950
COPYRIGHT 1999 DERWENT INFORMATION LTD
TITLE: Production of antibodies from cells with modified immunoglobulin locus - generated by Cre-mediated site-specific recombination to provide increased recombination efficiency
INVENTOR: JAKOBOVITS, A; ZSEBO, K M

PRIORITY-DATA:
1995US-0412826

March 29, 1995

PATENT-FAMILY:
PUB-NO

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
KR 98703366 A	October 15, 1998	N/A	000	C12N005/00
WO 9630498 A1	October 3, 1996	E	060	C12N005/00
AU 9655310 A	October 16, 1996	N/A	000	C12N005/00
EP 817835 A1	January 14, 1998	E		

JP 11503015 W
March 23, 1999

000 C12N005/00
N/A
048 C12N015/09

AU 707813 B
July 22, 1999
N/A
000 C12N005/00

INT-CL (IPC): C12 N 5/00; C12 N 5/06; C12 N 5/10; C12 N 5/16; C12 N 15/00; C12 N 15/06; C12 N 15/09; C12 N 15/13; C12 P 21/02

ABSTRACTED-PUB-NO: WO 9630498A
BASIC-ABSTRACT:

A cell expressing an antibody (Ab) from a genomic sequence contg. a modified immunoglobulin (Ig) locus, is produced using Cre-mediated site-specific recombination to modify the locus by: (a) transfecting an Ab-producing cell with a first homology-targeting vector contg. a first lox site and a targeting sequence homologous to a first DNA sequence adjacent to the region of the Ig locus to be modified, so that the lox site is inserted into the genomic sequence via site-specific homologous recombination with genomic DNA in vivo; (b) transfecting the cell with a lox-targeting vector comprising a second lox site suitable for Cre-mediated recombination with the first lox site, and a sequence to modify the Ig locus; (c) interacting the lox sites with Cre so that the modifying sequence inserts into the genomic sequence via Cre-mediated site-specific recombination of the lox sites, thus modifying the Ig locus; and (d) selecting a transfectant with a modified Ig locus which produces the Ab.

USE - The method allows the prodn. of cells expressing modified Ab, e.g. having the constant or variable region modified, for class-switching an Ab or to alter the antigen specificity of the Ab.

ADVANTAGE - The method provides increased efficiency of recombination (Cre-mediated recombination ranges from 2-3% recombination events) over previous methods of modifying Ig loci directly in Ab-producing cells using only homologous recombination for modifying the loci (ca. 0.39-0.75% recombination).

85. Document ID: US 5945339 A, WO 9622364 A1, AU 9646960 A, US 5780296 A, EP 873402 A1
Entry 85 of 88

File: DWPI

Aug 31, 1999

DERWENT-ACC-NO: 1996-354521
DERWENT-WEEK: 199942
COPYRIGHT 1999 DERWENT INFORMATION LTD
TITLE: Isolated recombinase enzyme and gene - obtd. from Ustilago maydis, used to promote homologous recombination in eukaryotic cells
INVENTOR: HOLLOWMAN, W K; KMIEC, E B

PRIORITY-DATA:
1995US-0373134

January 17, 1995

1998US-0114637
July 13, 1998

PATENT-FAMILY:
PUB-NO

PUB-DATE

LANGUAGE

PAGES

MAIN-IPC

US 5945339 A
August 31, 1999
N/A
000 C12N015/64

WO 9622364 A1
July 25, 1996
E
071 C12N009/00

AU 9646960 A
August 7, 1996
N/A
000 C12N009/00

US 5780296 A
July 14, 1998
N/A
000 C12N015/63

EP 873402 A1
October 28, 1998
E
000 C12N009/00

INT-CL (IPC): C12 N 9/00; C12 N 9/22; C12 N 15/63; C12 N 15/64

ABSTRACTED-PUB-NO: US 5780296A
BASIC-ABSTRACT:

Novel isolated protein (A): (a) is an ATPase having an apparent mol.wt. by SDS-PAGE of greater than 70 kD; (b) catalyses the formation of complementary or identical strand pairings of polydeoxynucleic acids (PDAs); (c) promotes homologous recombination (HR) in a eukaryote; and (d) has a sequence contg. the tetrapeptide (I): (Ser/Thr)-Pro-Xaa-(Arg/Lys) (I), Xaa = any amino acid.

USE - The prods. and methods can be used to promote HR in cells for, e.g. making specific genetic alterations in cells to produce a recombinant protein, introducing specific alterations in embryonic stem cells or ova to be used in the construction of transgenic animals, modifying in vitro explanted tissue stem cells, e.g. haematopoietic stem cells, which can then be continued in culture or reimplanted into a non-human host to produce a specific prod. or reimplanted into a human subject in need of gene therapy for a medical condition.

ABSTRACTED-PUB-NO:

US 5945339A EQUIVALENT-ABSTRACTS:

Novel isolated protein (A): (a) is an ATPase having an apparent mol.wt. by SDS-PAGE of greater than 70 kD; (b) catalyses the formation of complementary or identical strand pairings of polydeoxynucleic acids (PDAs); (c) promotes homologous recombination (HR) in a eukaryote; and (d) has a sequence contg. the tetrapeptide (I): (Ser/Thr)-Pro-Xaa-(Arg/Lys) (I), Xaa = any amino acid.

USE - The prods. and methods can be used to promote HR in cells for, e.g.

making specific genetic alterations in cells to produce a recombinant protein, introducing specific alterations in embryonic stem cells or ova to be used in the construction of transgenic animals, modifying in vitro explanted tissue stem cells, e.g. haematopoietic stem cells, which can then be continued in culture or reimplanted into a non-human host to produce a specific prod. or reimplanted into a human subject in need of gene therapy for a medical condition.

Novel isolated protein (A): (a) is an ATPase having an apparent mol.wt. by SDS-PAGE of greater than 70 kD; (b) catalyses the formation of complementary or identical strand pairings of polydeoxynucleic acids (PDAs); (c) promotes homologous recombination (HR) in a eukaryote; and (d) has a sequence contg. the tetrapeptide (I): (Ser/Thr)-Pro-Xaa-(Arg/Lys) (I), Xaa = any amino acid.

USE - The prods. and methods can be used to promote HR in cells for, e.g. making specific genetic alterations in cells to produce a recombinant protein, introducing specific alterations in embryonic stem cells or ova to be used in the construction of transgenic animals, modifying in vitro explanted tissue stem cells, e.g. haematopoietic stem cells, which can then be continued in culture or reimplanted into a non-human host to produce a specific prod. or reimplanted into a human subject in need of gene therapy for a medical condition.

WO 9622364A

86. Document ID: US 5910415 A, WO 9417176 A1, EP 686191 A1, US 5527695 A, US 5744336 A
Entry 86 of 88

File: DWPI

Jun 8, 1999

DERWENT-ACC-NO: 1994-264090
DERWENT-WEEK: 199930
COPYRIGHT 1999 DERWENT INFORMATION LTD
TITLE: DNA constructs - for creating transgenic eukaryotic cells
INVENTOR: HODGES, T K; LYZNIK, L A

PRIORITY-DATA:

1993US-0010997	January 29, 1993
1996US-0612551	March 8, 1996
1998US-0006232	January 13, 1998

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 5910415 A	June 8, 1999	N/A	000	C12Q001/68
WO 9417176 A1	August 4, 1994	E	079	C12N005/00
EP 686191 A1	December 13, 1995			

E	000	C12N005/00
US 5527695 A	June 18, 1996	N/A
US 5744336 A	April 28, 1998	N/A
	027	C12N015/00
	028	C07H021/04

INT-CL (IPC): A01 H 1/04; A01 H 4/00; A01 H 5/00; A01 H 5/10; C07 H 21/04; C12 N 5/00 ; C12 N 15/00; C12 N 15/09; C12 N 15/63; C12 N 15/82; C12 Q 1/68

ABSTRACTED-PUB-NO: US 5527695A
BASIC-ABSTRACT:

The following are new: (1) a DNA construct (I) for transforming a eukaryotic cell comprising: (a) a multifunctional DNA sequence comprising: (i) a gene encoding a selectable marker operably linked to (ii) regulatory sequences for eukaryotic gene expression; and (iii) a sequence of interest flanked by (iv) sequences homologous to eukaryotic cell sequences; and (b) a pair of directly repeating site-specific (s-s) recombination sequences; (2) a DNA construct (II) for inserting a DNA sequence of interest into eukaryotic cell DNA comprising a multifunctional DNA sequence comprising: (i) a gene encoding a 1st s-s recombinase capable of recognising 1st s-s recombination sequences; (ii) a DNA sequence targeted for inversion via homologous recombination into eukaryotic cell DNA, comprising a sequence of interest and excisable selection region and flanked by: (iii) a sequence homologous to eukaryotic cell sequences, where the excisable selection region comprises a gene encoding a selectable marker and a gene encoding a 2nd s-s recombinase capable of recognising a 2nd s-s recombination sequence, both genes capable of eukaryotic gene expression, and the excisable region is flanked by: (iv) a pair of directly repeating s-s recombination sequences; and (3) a DNA construct (III) for transforming eukaryotic cells comprising: (a) a multifunctional DNA sequence comprising: (i) a gene encoding a selectable marker operably linked to (ii) regulatory sequences for eukaryotic gene expression; (iii) a DNA sequence targeted for inversion into the eukaryotic cell having less than or equal to 1 polylinker region and flanked by: (iv) nucleotide sequences homologous to eukaryotic cell sequences; and (b) a flanking pair of directly-repeated s-s recombination sequences.

Also claimed are: (4) a plant entity comprising a plant cell, seed or plant, produced from the in vitro introduction of an exogenous DNA fragment into a plant cell; (5) a method for directly selecting for insertion of a DNA sequence of interest into a specific sequence of an organism's DNA comprising: (a) introducing (II) into an organism's cells; (b) applying selection means to isolate cells contg. (II) integrated into cellular DNA; (c) removing randomly inserted DNA constructs; (d) applying selection means to isolate cells having the targeted DNA sequence integrated into the organism's DNA via a homologous recombination event; (e) removing the excisable selection region; and (f) culturing the resultant cells to regenerate an entire organism; and (6) a kit contg. (III) and an inducer cpd. capable of inducing

an inducible promoter.

USE - (I) can be used to target a DNA sequence of interest into a specific site of a host cell's DNA. (II) is useful for directly selecting for insertion of a DNA sequence of interest into a specific sequence of an organism's DNA. Fertile, transgenic plants can be produced (claimed) contg. a DNA sequence of interest, utilising (I), (II) or (III).
ABSTRACTED-PUB-NO:

US 5744336A EQUIVALENT-ABSTRACTS:

A method for the production of fertile, transgenic plants wherein the transgenic plant has a DNA sequence of interest integrated at a predetermined DNA sequence of the plant, said method comprising the steps of

introducing into plant cells a DNA construct comprising

a multifunctional DNA sequence flanked by a pair of directly repeated site-specific recombination sequences,

said multifunctional DNA sequence comprising a gene encoding a selectable marker, and a DNA sequence of interest,

wherein said DNA sequence of interest is flanked by nucleotide sequences sharing homology to the predetermined nucleotide sequence present in the plant cell, and the selectable marker gene is operably linked to regulatory sequences capable of expressing the gene in the plant cell,

selecting for plant cells having said DNA construct integrated into the DNA of the plant cell,

eliminating randomly inserted DNA constructs through expression of a recombinase gene capable of initiating recombination at the site-specific recombinase sequences in the plant cells,

identifying cells having said DNA sequence of interest integrated into the plant's DNA via a homologous recombination event, and

culturing said identified cells to generate an entire plant.

The following are new: (1) a DNA construct (I) for transforming a eukaryotic cell comprising: (a) a multifunctional DNA sequence comprising: (i) a gene encoding a selectable marker operably linked to (ii) regulatory sequences for eukaryotic gene expression; and (iii) a sequence of interest flanked by (iv) sequences homologous to eukaryotic cell sequences; and (b) a pair of directly repeating site-specific (s-s) recombination sequences; (2) a DNA construct (II) for inserting a DNA sequence of interest into eukaryotic cell DNA comprising a multifunctional DNA sequence comprising: (i) a gene encoding a 1st s-s recombinase capable of recognising 1st s-s recombination sequences; (ii) a DNA sequence targeted for inversion via homologous recombination into eukaryotic cell DNA, comprising a sequence of interest and excisable selection region and flanked by: (iii) a sequence homologous to eukaryotic cell sequences, where the excisable selection region comprises a gene encoding a selectable marker and a gene encoding a 2nd s-s recombinase capable of recognising a 2nd s-s recombination sequence, both genes capable of eukaryotic gene expression, and the excisable region is flanked by: (iv) a pair of directly repeating s-s recombination sequences; and (3) a DNA construct (III) for

transforming eukaryotic cells comprising: (a) a multifunctional DNA sequence comprising: (i) a gene encoding a selectable marker operably linked to (ii) regulatory sequences for eukaryotic gene expression; (iii) a DNA sequence targeted for inversion into the eukaryotic cell having less than or equal to 1 polylinker region and flanked by: (iv) nucleotide sequences homologous to eukaryotic cell sequences; and (b) a flanking pair of directly-repeated s-s recombination sequences.

Also claimed are: (4) a plant entity comprising a plant cell, seed or plant, produced from the in vitro introduction of an exogenous DNA fragment into a plant cell; (5) a method for directly selecting for insertion of a DNA sequence of interest into a specific sequence of an organism's DNA comprising: (a) introducing (II) into an organism's cells; (b) applying selection means to isolate cells contg. (II) integrated into cellular DNA; (c) removing randomly inserted DNA constructs; (d) applying selection means to isolate cells having the targeted DNA sequence integrated into the organism's DNA via a homologous recombination event; (e) removing the excisable selection region; and (f) culturing the resultant cells to regenerate an entire organism; and (6) a kit contg. (III) and an inducer cpd. capable of inducing an inducible promoter.

USE - (I) can be used to target a DNA sequence of interest into a specific site of a host cell's DNA. (II) is useful for directly selecting for insertion of a DNA sequence of interest into a specific sequence of an organism's DNA. Fertile, transgenic plants can be produced (claimed) contg. a DNA sequence of interest, utilising (I), (II) or (III).

US 5910415A

The following are new: (1) a DNA construct (I) for transforming a eukaryotic cell comprising: (a) a multifunctional DNA sequence comprising: (i) a gene encoding a selectable marker operably linked to (ii) regulatory sequences for eukaryotic gene expression; and (iii) a sequence of interest flanked by (iv) sequences homologous to eukaryotic cell sequences; and (b) a pair of directly repeating site-specific (s-s) recombination sequences; (2) a DNA construct (II) for inserting a DNA sequence of interest into eukaryotic cell DNA comprising a multifunctional DNA sequence comprising: (i) a gene encoding a 1st s-s recombinase capable of recognising 1st s-s recombination sequences; (ii) a DNA sequence targeted for inversion via homologous recombination into eukaryotic cell DNA, comprising a sequence of interest and excisable selection region and flanked by: (iii) a sequence homologous to eukaryotic cell sequences, where the excisable selection region comprises a gene encoding a selectable marker and a gene encoding a 2nd s-s recombinase capable of recognising a 2nd s-s recombination sequence, both genes capable of eukaryotic gene expression, and the excisable region is flanked by: (iv) a pair of directly repeating s-s recombination sequences; and (3) a DNA construct (III) for transforming eukaryotic cells comprising: (a) a multifunctional DNA sequence comprising: (i) a gene encoding a selectable marker operably linked to (ii) regulatory sequences for eukaryotic gene expression; (iii) a DNA sequence targeted for inversion into the eukaryotic cell having less than or equal to 1 polylinker region and flanked by: (iv) nucleotide sequences homologous to eukaryotic cell

sequences; and (b) a flanking pair of directly-repeated s-s recombination sequences.

Also claimed are: (4) a plant entity comprising a plant cell, seed or plant, produced from the in vitro introduction of an exogenous DNA fragment into a plant cell; (5) a method for directly selecting for insertion of a DNA sequence of interest into a specific sequence of an organism's DNA comprising: (a) introducing (II) into an organism's cells; (b) applying selection means to isolate cells contg. (II) integrated into cellular DNA; (c) removing randomly inserted DNA constructs; (d) applying selection means to isolate cells having the targeted DNA sequence integrated into the organism's DNA via a homologous recombination event; (e) removing the excisable selection region; and (f) culturing the resultant cells to regenerate an entire organism; and (6) a kit contg. (III) and an inducer cpd. capable of inducing an inducible promoter.

USE - (I) can be used to target a DNA sequence of interest into a specific site of a host cell's DNA. (II) is useful for directly selecting for insertion of a DNA sequence of interest into a specific sequence of an organism's DNA. Fertile, transgenic plants can be produced (claimed) contg. a DNA sequence of interest, utilising (I), (II) or (III).

WO 9417176A

87. Document ID: US 5763240 A, WO 9322443 A1, AU 9341156 A, JP 07506252 W, EP 672159 A1
Entry 87 of 88

File: DWPI

Jun 9, 1998

DERWENT-ACC-NO: 1993-368802
DERWENT-WEEK: 199830
COPYRIGHT 1999 DERWENT INFORMATION LTD
TITLE: In vivo homologous sequence targeting in eukaryotic cells - using a targeting polynucleotide and recombinase to deliver agents or alter genes
INVENTOR: SENA, E P; ZARLING, D A

PRIORITY-DATA:
1992US-0939767

September 2, 1992

1992US-0873438

April 24, 1992

1994US-0275916

July 14, 1994

PATENT-FAMILY:
PUB-NO

PUB-DATE

LANGUAGE

PAGES

MAIN-IPC

US 5763240 A

June 9, 1998

N/A

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C12N015/64

WO 9322443 A1

November 11, 1993

E

100

C12N015/90

AU 9341156 A

November 29, 1993

N/A

000

C12N015/90

JP 07506252 W

July 13, 1995

N/A

027

C12N015/09

EP 672159 A1

September 20, 1995

E

000

C12N015/90

INT-CL (IPC): A01 K 67/027; A61 K 48/00; C12 N 5/10; C12 N 15/09; C12 N 15/64; C12 N 15/90; C12 P 19/34; C12 Q 1/68; G01 N 33/68

ABSTRACTED-PUB-NO: US 5763240A
BASIC-ABSTRACT:

A method is claimed for targeting and altering, by homologous recombination, a pre-selected target DNA sequence in a eukaryotic cell to make a targeted sequence modification, comprising (a) introducing into at least one eukaryotic cell at least one recombinase and at least one targeting polynucleotide having a homology clamp that corresponds to or is complementary to a preselected target DNA sequence and (b) identifying a eukaryotic cell having a targeted DNA sequence modification at a preselected target DNA sequence. Also claimed are (A) a compsn. for producing a targeted modification of an endogenous DNA sequence, comprising a targeting polynucleotide and a recombinase; (B) a compsn. for producing a targeted sequence modification of a human disease allele; a targeting polynucleotide contg. a corrected sequence a recombinase or an expression polynucleotide that encodes and expresses a recombinase; (C) a kit for therapy, monitoring or prophylaxis of a genetic disease comprising a recombinase and a targeting polynucleotide; (D) a method for treating a disease of an animal harbouring a disease allele, comprising administering a compsn. consisting of: (a) a recombinase or an expression polynucleotide encoding a recombinase and (b) a targeting polynucleotide which produces a sequence modification upon homologous recombination with the disease allele; (E) an animal comprising an allele that has a sequence modification as in (D).

USE/ADVANTAGE - The method can be used to target chemical substituents (e.g. drugs) in a sequence-specific manner in vivo, to correct or to generate genetic mutations in endogenous DNA sequence by homologous recombination and/or gene conversion or to produce homologously targeted transgenic animals at high efficiency. In partic., the method can be used for correcting disease alleles involved in human genetic diseases such as inherited genetic disease (e.g. cystic fibrosis) and neoplasm for treating or preventing viral diseases, by HBV hepatitis.

ABSTRACTED-PUB-NO:

WO 9322443A EQUIVALENT-ABSTRACTS:

A method is claimed for targeting and altering, by homologous recombination, a pre-selected target DNA sequence in a eukaryotic cell to make a targeted sequence modification, comprising (a) introducing into at least one eukaryotic cell at least one recombinase and at least one targeting polynucleotide having a homology clamp that corresponds to or is complementary to a preselected

target DNA sequence and (b) identifying a eukaryotic cell having a targeted DNA sequence modification at a preselected target DNA sequence. Also claimed are (A) a compsn. for producing a targeted modification of an endogenous DNA sequence, comprising a targeting polynucleotide and a recombinase; (B) a compsn. for producing a targeted sequence modification of a human disease allele; a targeting polynucleotide contg. a corrected sequence a recombinase or an expression polynucleotide that encodes and expresses a recombinase; (C) a kit for therapy, monitoring or prophylaxis of a genetic disease comprising a recombinase and a targeting polynucleotide; (D) a method for treating a disease of an animal harbouring a disease allele, comprising administering a compsn. consisting of: (a) a recombinase or an expression polynucleotide encoding a recombinase and (b) a targeting polynucleotide which produces a sequence modification upon homologous recombination with the disease allele; (E) an animal comprising an allele that has a sequence modification as in (D).

USE/ADVANTAGE - The method can be used to target chemical substits. (e.g. drugs) in a sequence-specific manner in vivo, to correct or to generate genetic mutations in endogenous DNA sequence by homologous recombination and/or gene conversion or to produce homologously targeted transgenic animals at high efficiency. In partic., the method can be used for correcting disease alleles involved in human genetic diseases such as inherited genetic disease (e.g. cystic fibrosis) and neoplasm for treating or preventing viral diseases, by HBV hepatitis.

88. Document ID: EP 542466 A2, AU 655512 B, AU 9228316 A, CA 2082577 A, EP 542466 A3, JP 05336977 A, NZ 245070 A, ZA 9208662 A
Entry 88 of 88

File: DWPI

May 19, 1993

DERWENT-ACC-NO: 1993-160938
DERWENT-WEEK: 199320
COPYRIGHT 1999 DERWENT INFORMATION LTD
TITLE: Baculovirus transfer vector contg. locus of crossover PI sequence - as substrate for recombinase enzyme, provides efficient homologous recombination with recombinant virus, esp. for expression of polypeptide(s) for vaccines
INVENTOR: GEWERT, D R; PEAKMAN, T C

PRIORITY-DATA:
1991GB-0023929

November 11, 1991

PATENT-FAMILY:
PUB-NO

PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 542466 A2 May 19, 1993	E	018	C12N015/86
AU 655512 B December 22, 1994	N/A	000	

Pub No.	Date	Language	Pages	IPC Class.
AU 9228316 A	May 13, 1993	N/A	000	C12N015/86
CA 2082577 A	May 12, 1993	N/A	000	C12N015/86
EP 542466 A3	October 6, 1993	N/A	000	C12N015/86
JP 05336977 A	December 21, 1993	N/A	015	C12N015/86
NZ 245070 A	November 25, 1994	N/A	000	C12N015/86
ZA 9208662 A	July 27, 1994	N/A	036	C12N000/00

INT-CL (IPC): A61K 39/00; A61K 39/12; C12N 0/00; C12N 5/10; C12N 7/01; C12N 15/64; C12N 15/74; C12N 15/86; G01N 33/53

ABSTRACTED-PUB-NO: EP 542466A
BASIC-ABSTRACT:

New baculovirus transfer vector contains a restriction site for insertion of a DNA sequence (I) encoding a heterologous polypeptide (II); regulatory elements for expression of (I) when inserted and a loXP (locus of crosslover PI) DNA sequence (III) to act as substrate for the Cre (causes recombination) recombinase protein (N).

Also new are (1) recombinant DNA (V) comprising this vector and (I); (2) a baculovirus contg. (III) as substrate for (IV); (3) recombinant baculovirus prepd. by homologous recombination of the virus (2) and (V); (4) insect cells transfected with the recombinant virus; (5) vaccines contg. (II) prepd. by culturing the transfected insect cells; and (6) test kits for detecting (II)-specific antibodies or (II) themselves.

(III) is esp. of formula

5'-CCTTAATATAACTTCGTATAP
TGTATGCTATACGAAGTTATTAGGTCG 3'-GGAATTATATTGA
AGCATATTACA
TACGATATGCTTCAATAATCCAGC

USE/ADVANTAGE - The transfected cells provide high level expression of (II) which are useful in human or veterinary medicine; in vaccines and in diagnostic assays. The transfer vector provides an efficient in vitro system for constructing recombinant viruses which can be identified and isolated. Up to 50 million recombinants can be produced from 1 microg plasmid DNA and up to 50% of viral progeny are recombinants. If required inserted genes are easily recovered and reinserted, and recombination efficiency is independent of gene size (which can be 10kb or larger).

Term	Documents
1 SAME 2	88

including document number

Display Format:

09/203500
Att #11

1. Document ID: US 6087107 A

L3: Entry 1 of 58

File: USPT

Jul 11, 2000

US-PAT-NO: 6087107

DOCUMENT-IDENTIFIER: US 6087107 A

TITLE: Therapeutics and diagnostics for congenital heart disease based on a novel human transcription factor
DATE-ISSUED: July 11, 2000

US-CL-CURRENT: 435/6; 435/7.1, 536/24.31, 536/24.33

APPL-NO: 9/ 083351

DATE FILED: May 22, 1998

PARENT-CASE:

This application claims priority to provisional patent application 60/081,870, filed Apr. 15, 1998.

IN: Sheffield; Val C., Alward; Wallace L. M., Stone; Edwin M., Nishimura; Darryl, Patil; Shiva

AB: Methods and compositions for treating a congenital heart disease and methods and compositions for prognosing or diagnosing a congenital heart disease in a subject are disclosed.

2. Document ID: US 6074853 A

L3: Entry 2 of 58

File: USPT

Jun 13, 2000

US-PAT-NO: 6074853

DOCUMENT-IDENTIFIER: US 6074853 A

TITLE: Sequence alterations using homologous recombination
DATE-ISSUED: June 13, 2000

US-CL-CURRENT: 435/91.1; 435/455, 435/471

APPL-NO: 9/ 133934

DATE FILED: August 14, 1998

PARENT-CASE:

CROSS-REFERENCE TO RELATED APPLICATIONS This is a continuing application of U.S. application Ser. No. 08/910,367, filed Aug. 13, 1997 now U.S. Pat. No. 5,948,653, and claims the benefit of U.S. Provisional Application No. 60/041,173, filed Mar. 21, 1997.

IN: Pati; Sushma, Zarling; David A.

AB: The invention relates to methods for targeting an exogenous polynucleotide or exogenous complementary polynucleotide pair to a predetermined endogenous DNA target sequence in a target cell by homologous pairing, particularly for altering an endogenous DNA sequence, such as a chromosomal DNA sequence, typically by targeted homologous recombination. In certain embodiments, the invention relates to methods

for targeting an exogenous polynucleotide having a linked chemical substituent to a predetermined endogenous DNA sequence in a metabolically active target cell, generating a DNA sequence-specific targeting of one or more chemical substituents in an intact nucleus of a metabolically active target cell, generally for purposes of altering a predetermined endogenous DNA sequence in the cell. The invention also relates to compositions that contain exogenous targeting polynucleotides, complementary pairs of exogenous targeting polynucleotides, chemical substituents of such polynucleotides, and recombinase proteins used in the methods of the invention.

3. Document ID: US 6066778 A

L3: Entry 3 of 58

File: USPT

May 23, 2000

US-PAT-NO: 6066778

DOCUMENT-IDENTIFIER: US 6066778 A

TITLE: Transgenic mice expressing APC resistant factor V
DATE-ISSUED: May 23, 2000

US-CL-CURRENT: 424/9.2

APPL-NO: 8/ 746111

DATE FILED: November 6, 1996

IN: Ginsburg; David, Cui; Jisong

AB: The present invention relates to compositions and methods for the screening of compounds for anticoagulant activity. In particular, the present invention relates to non-human transgenic animals expressing activated protein C ("APC")-resistant factor V proteins which display a predisposition toward spontaneous thrombosis. The present invention also provides methods for using these transgenic animals to screen compounds for anticoagulant activity.

4. Document ID: US 6046308 A

L3: Entry 4 of 58

File: USPT

Apr 4, 2000

US-PAT-NO: 6046308

DOCUMENT-IDENTIFIER: US 6046308 A

TITLE: Isolated TRBP polypeptides and uses therefor
DATE-ISSUED: April 4, 2000

US-CL-CURRENT: 530/350

APPL-NO: 9/ 360220

DATE FILED: July 23, 1999

PARENT-CASE:

RELATED APPLICATIONS This application is a divisional of U.S. patent application Ser. No. 08/840,164, which was filed on Apr. 11, 1997.

IN: Glucksmann; M. Alexandra

AB: The invention provides nucleic acids encoding a TRBP polypeptide, fragments thereof and homologs thereof The invention also provides TRBP polypeptides, fragments thereof and homologs thereof, and TRBP binding proteins. Methods for treating diseases or conditions characterized by an aberrant TRBP activity, e.g., by administering to the subject a TRBP therapeutic, are also disclosed. Diseases or conditions that can be treated according to the methods of the invention include thyroid-related disorders, metabolic disorders, and diabetes. Also disclosed are methods for predicting whether a subject is at risk of developing a disease associated with an aberrant TRBP activity, by determining, e.g., whether the subject has a genetic lesion in a TRBP gene and assays for identifying TRBP therapeutics.

5. Document ID: US 6037173 A

L3: Entry 5 of 58

File: USPT

Mar 14, 2000

US-PAT-NO: 6037173
DOCUMENT-IDENTIFIER: US 6037173 A
TITLE: Isolated nucleic acid encoding TRBP
DATE-ISSUED: March 14, 2000

US-CL-CURRENT: 435/325; 435/320.1, 435/366, 536/23.1, 536/23.5, 536/24.31

APPL-NO: 8/ 840146
DATE FILED: April 11, 1997

IN: Glucksmann; M. Alexandra

AB: The invention provides nucleic acids encoding a TRBP polypeptide, fragments thereof and homologs thereof The invention also provides TRBP polypeptides, fragments thereof and homologs thereof, and TRBP binding proteins. Methods for treating diseases or conditions characterized by an aberrant TRBP activity, e.g., by administering to the subject a TRBP therapeutic, are also disclosed. Diseases or conditions that can be treated according to the methods of the invention include thyroid-related disorders, metabolic disorders, and diabetes. Also disclosed are methods for predicting whether a subject is at risk of developing a disease associated with an aberrant TRBP activity, by determining, e.g., whether the subject has a genetic lesion in a TRBP gene and assays for identifying TRBP therapeutics.

6. Document ID: US 6031076 A

L3: Entry 6 of 58

File: USPT

Feb 29, 2000

US-PAT-NO: 6031076
DOCUMENT-IDENTIFIER: US 6031076 A
TITLE: Conservin compositions
DATE-ISSUED: February 29, 2000

US-CL-CURRENT: 530/350; 530/402, 536/23.1, 536/23.4, 536/23.5

APPL-NO: 9/ 002832
DATE FILED: January 5, 1998

PARENT-CASE:
RELATED APPLICATIONS This application is a divisional application of U.S. Ser. No. 08/688,609, filed on Jul. 30, 1996, now U.S. Pat. No. 5,807,708 of all of the aforementioned application(s) are hereby incorporated by reference.

IN: Falb; Dean A., Gimeno; Carlos J.

AB: The present invention relates to the discovery of novel conservin genes and polypeptides. Therapeutics, diagnostics and screening assays based on these molecules are also disclosed.

7. Document ID: US 6015692 A

L3: Entry 7 of 58

File: USPT

Jan 18, 2000

US-PAT-NO: 6015692
DOCUMENT-IDENTIFIER: US 6015692 A
TITLE: CDC37 cell-cycle regulatory protein and uses related thereto
DATE-ISSUED: January 18, 2000

US-CL-CURRENT: 435/69.1; 435/183, 435/252.3, 435/320.1, 435/325, 536/23.2

APPL-NO: 8/ 853733
DATE FILED: May 9, 1997

PARENT-CASE:
RELATED APPLICATIONS This application is a continuation of U.S. Ser. No. 08/625,209 filed Apr. 1, 1996, now U.S. Pat. No. 5,756,671, which is a continuation-in-part of U.S. Ser. No. 08/466,679 filed Jun. 6, 1995, entitled "Cdc37 Cell-Cycle Regulatory Protein and Uses Related Thereto", now abandoned, which is a continuation-in-part of U.S. Ser. No. 08/253,155 filed Jun. 2, 1994, entitled "CDK4 Binding Proteins" now U.S. Pat. No. 5,691,147. The teachings of both U.S. Ser. Nos. 08/253,155 and 08/466,679 are incorporated herein by reference.

IN: Gyuris; Jeno, Lamphere; Lou, Draetta; Giulio

AB: The present invention relates to the discovery in mammalian cells, particularly human cells, of a novel CDK-binding protein, referred to herein as "cdc37". As described herein, this protein functions to facilitate activation and accordingly functions in the modulation of cell-cycle progression, and therefore ultimately of cell growth and differentiation. Moreover, binding data indicated that cdc37 may function coordinately with other cell-cycle regulatory proteins, such as of cyclin-dependent kinases (CDKs), src, p53 and erk kinases.

8. Document ID: US 6008014 A

L3: Entry 8 of 58

File: USPT

Dec 28, 1999

US-PAT-NO: 6008014
DOCUMENT-IDENTIFIER: US 6008014 A
TITLE: Method of making lipid metabolic pathway compositions
DATE-ISSUED: December 28, 1999

US-CL-CURRENT: 435/69.1; 435/325, 435/455, 435/91.1, 536/23.1

APPL-NO: 8/ 707399
DATE FILED: September 4, 1996

IN: Gimeno; Carlos J., Acton; Susan

AB: The present invention relates to the discovery of novel genes encoding Lipid Metabolic Pathway (LMP) polypeptides. Therapeutics, diagnostics and screening assays based on these molecules are also disclosed.

9. Document ID: US 6001619 A

L3: Entry 9 of 58

File: USPT

Dec 14, 1999

US-PAT-NO: 6001619
DOCUMENT-IDENTIFIER: US 6001619 A
TITLE: Ubiquitin ligases, and uses related thereto
DATE-ISSUED: December 14, 1999

US-CL-CURRENT: 435/193; 536/23.2

APPL-NO: 8/ 539205
DATE FILED: October 4, 1995

IN: Beach; David, Caligiuri; Maureen G., Nefsky; Bradley

AB: The present invention relates to the discovery in eukaryotic cells of a ubiquitin ligases. These proteins are referred to herein collectively as "pub"

proteins for Protein Ubiquitin ligase, and individually as h-pub1, h-pub2 and s-pub1 for the human pub1 and pub2 and Schizosaccharomyces pombe pub1 clones, respectively. Pub1 proteins apparently play a role in the ubiquitination of the mitotic activating tyrosine phosphatase cdc25, and thus they may regulate the progression of proliferation in eukaryotic cells by activating the cyclin dependent kinase complexes. In S. pombe, disruption of s-pub1 elevates the level of cdc25 protein in vivo increasing the activity of the tyrosine kinases, wee1 and mik1, required to arrest the cell-cycle. Loss of wee1 function in an S. pombe cell carrying a disruption in the s-pub1 gene results in a lethal premature entry into mitosis; such lethal phenotype can be rescued by the loss of cdc25 function. An ubiquitin thioester adduct of s-pub1 can be isolated from S. pombe and disruption of s-pub1 dramatically reduces ubiquitination of cdc25.

10. Document ID: US 5994070 A

L3: Entry 10 of 58

File: USPT

Nov 30, 1999

US-PAT-NO: 5994070
DOCUMENT-IDENTIFIER: US 5994070 A
TITLE: Trio molecules and uses related thereto
DATE-ISSUED: November 30, 1999

US-CL-CURRENT: 435/6; 435/320.1, 435/325, 435/69.1, 536/23.5, 536/24.31

APPL-NO: 8/ 826267
DATE FILED: March 27, 1997

PARENT-CASE:
This application claims the benefit of U.S. Provisional Application No. 60/014,214 filed Mar. 27, 1996.

IN: Streuli; Michel, Debant; Anne, Serra-Pages; Carles

AB: Nucleic acids encoding TRIO proteins, the TRIO proteins themselves, and active portions thereof as described. In addition, antibodies immunoreactive with TRIO proteins, and preparations of such compositions are provided. Diagnostic and therapeutic assays and reagents for detecting and treating disorders involving, for example, aberrant expression (or loss thereof) of the TRIO protein are described. Assays are provided for identifying agents that modulate the biological function of TRIO proteins.

11. Document ID: US 5989804 A

L3: Entry 11 of 58

File: USPT

Nov 23, 1999

US-PAT-NO: 5989804
DOCUMENT-IDENTIFIER: US 5989804 A
TITLE: E6 binding proteins
DATE-ISSUED: November 23, 1999

US-CL-CURRENT: 435/5, 435/7.23, 435/7.6, 435/7.7, 435/7.71,
435/7.72, 435/7.92, 514/12, 530/300,
530/350, 536/23.5, 536/23.72, 930/220

APPL-NO: 8/ 555722
DATE FILED: November 14, 1995

PARENT-CASE:
RELATED APPLICATIONS This application is a continuation-in-part of
U.S. Ser. No. 08/273,059,
entitled "E6 Binding Proteins" which was filed on Jul. 8, 1994, now
abandoned, the specification
of which are incorporated by reference herein .

IN: Androphy; Elliot J., Chen; Jason J.

AB: E6-BP polypeptides, nucleic acids encoding E6-BP
polypeptides, and uses thereof.

12. Document ID: US 5981702 A

L3: Entry 12 of 58

File: USPT

Nov 9, 1999

US-PAT-NO: 5981702
DOCUMENT-IDENTIFIER: US 5981702 A
TITLE: Cyclin/CDK associated proteins, and uses related thereto
DATE-ISSUED: November 9, 1999

US-CL-CURRENT: 530/350

APPL-NO: 8/ 531439
DATE FILED: September 21, 1995

IN: Zhang; Hui, Beach; David

AB: The present invention relates to the discovery in mammalian
cells, particularly
human cells, of novel S-phase kinase associated proteins, p19 and p45,
referred to herein as
"Skp". As described herein, these proteins are components of the tumor
cell-specific cyclin
A/CDK2 complex and function to facilitate DNA replication. Interference
with p45 function in
vivo prevented entry into S-phase in both normal and transformed cells.
Binding data
indicated that p45 and p19 associate with each other in a binary complex.
Moreover, p45 is
required for p19 binding to cyclin A/CDK2.

13. Document ID: US 5968821 A

L3: Entry 13 of 58

File: USPT

Oct 19, 1999

US-PAT-NO: 5968821
DOCUMENT-IDENTIFIER: US 5968821 A
TITLE: Cell-cycle regulatory proteins, and uses related thereto
DATE-ISSUED: October 19, 1999

US-CL-CURRENT: 435/325; 435/320.1, 435/455, 435/6, 435/69.1,
536/23.1

APPL-NO: 8/ 893274
DATE FILED: July 15, 1997

PARENT-CASE:
RELATED APPLICATIONS This application is a continuation application
of Ser. No. 08/306,511 filed
on Sep. 14, 1994, which is a continuation-in-part of U.S. Ser. No.
08/248,812 filed May 25, 1994
and entitled "Cell-cycle Regulatory Protein, and Uses Related Thereto",
which is a
continuation-in-part of U.S. Ser. No. 08/227,371 filed Apr. 14, 1994 and
entitled "Cell-cycle
Regulatory Protein, and Uses Related Thereto", which is a
continuation-in-part of U.S. Ser. No.
08/154,915 filed Nov. 18, 1993 and entitled "Cyclin Complex
Rearrangements and Uses Related
Thereto", which is a continuation-in-part of U.S. Ser. No. 07/991,997 filed
Dec. 17, 1992 and
entitled "Cyclin Complex Rearrangements and Uses Related Thereto",
abandoned, which is a
continuation-in-part of U.S. Ser. No. 07/963,308 filed Oct. 16, 1992 and
entitled "D-Type Cyclin
and Uses Related Thereto". The teachings of U.S. Ser. Nos. 08/248,812,
08/227,371, 08/154,915,
07/991,997, 07/963,308 and related PCT publication US93/09945 are
incorporated herein by
reference.

IN: Beach; David H., Demetrick; Douglas J., Serrano; Manuel,
Hannon; Gregory J.

AB: The present invention relates to the discovery in eukaryotic
cells, particularly
mammalian cells, of a novel family of cell-cycle regulatory proteins
("CCR-proteins"). As
described herein, this family of proteins includes a polypeptide having an
apparent
molecular weight of 16 kDa, and a polypeptide having an apparent
molecular weight of
approximately 15 kDa, each of which can function as an inhibitor of
cell-cycle progression,
and therefore ultimately of cell growth. Thus, similar to the role of p21 to
the p53
checkpoint, the subject CCR-proteins may function coordinately with the
cell-cycle
regulatory protein, retinoblastoma (RB). Furthermore, the CCR-protein
family includes a
protein having an apparent molecular weight of 13.5 kDa (hereinafter
"p13.5"). The
presumptive role of p13.5, like p16 and p15, is in the regulation of the
cell-cycle.

14. Document ID: US 5965790 A

L3: Entry 14 of 58

File: USPT

Oct 12, 1999

US-PAT-NO: 5965790
DOCUMENT-IDENTIFIER: US 5965790 A
TITLE: SR-BI regulatory sequences and therapeutic methods of use
DATE-ISSUED: October 12, 1999

US-CL-CURRENT: 800/18; 435/29, 435/320.1, 435/325, 435/6, 536/24.1, 536/24.31, 800/21

APPL-NO: 8/ 812204
DATE FILED: March 6, 1997

IN: Acton; Susan Laurene

AB: The invention features nucleic acid molecules that are involved with (e.g. activate or regulate) human SR-BI receptor transcription, as well as complements thereto, and homologs thereof. In addition, drug discovery assays are provided for identifying agents which modulate SR-BI promoter activity and thereby modulate the expression of a gene regulated thereby. Such agents can be useful therapeutically for treating or preventing the development of a disease or condition that is caused or contributed to by an aberrant SR-BI activity. In a preferred embodiment, the disease or condition is characterized by inappropriate lipid transfer or metabolism (e.g., atherosclerosis or gallstone formation). Such agents can also be used to modulate expression of a specific gene under the control of the SR-BI promoter in gene therapy. Moreover, the present invention provides diagnostic assays and reagents for determining whether a subject has a disorder involving, for example, aberrant expression of SR-BI genes.

15. Document ID: US 5962316 A

L3: Entry 15 of 58

File: USPT

Oct 5, 1999

US-PAT-NO: 5962316
DOCUMENT-IDENTIFIER: US 5962316 A
TITLE: Cell-cycle regulatory proteins, and uses related thereto
DATE-ISSUED: October 5, 1999

US-CL-CURRENT: 435/325; 424/185.1, 424/93.21, 435/320.1, 435/455, 435/6, 435/69.1, 514/44, 530/350, 536/23.1, 536/23.4, 536/23.5, 536/24.1

APPL-NO: 8/ 306511
DATE FILED: September 14, 1994

PARENT-CASE:
RELATED APPLICATIONS This application is a continuation-in-part of U.S. Ser. No. 08/248,812 filed May 25, 1994 and entitled "Cell-cycle Regulatory Protein, and Uses Related Thereto", which is a continuation-in-part of U.S. Ser. No. 08/227,371 filed Apr. 14, 1994 and entitled "Cell-cycle Regulatory Protein, and Uses Related Thereto", which is a continuation-in-part of U.S. Ser. No. 08/154,915 filed Nov. 18, 1993 and entitled "Cyclin Complex Rearrangements and Uses Related

Thereto", which is a continuation-in-part of U.S. Ser. No. 07/991,997 filed Dec. 17, 1992 and entitled "Cyclin Complex Rearrangements and Uses Related Thereto", now abandoned, which is a continuation-in-part of U.S. Ser. No. 07/963,308 filed Oct. 16, 1992 and entitled "D-Type Cyclin and Uses Related Thereto". The teachings of U.S. Ser. Nos. 08/248,812, 08/227,371, 08/154,915, 07/991,997, 07/963,308 and related PCT publication US 93/09945 are incorporated herein by reference.

IN: Beach; David H., Demetrick; Douglas J., Serrano; Manuel, Hannon; Gregory J.

AB: The present invention relates to the discovery in eukaryotic cells, particularly mammalian cells, of a novel family of cell-cycle regulatory proteins ("CCR-proteins"). As described herein, this family of proteins includes a polypeptide having an apparent molecular weight of 16 kDa, and a polypeptide having an apparent molecular weight of approximately 15 kDa, each of which can function as an inhibitor of cell-cycle progression, and therefore ultimately of cell growth. Thus, similar to the role of p21 to the p53 checkpoint, the subject CCR-proteins may function coordinately with the cell-cycle regulatory protein, retinoblastoma (RB). Furthermore, the CCR-protein family includes a protein having an apparent molecular weight of 13.5 kDa (hereinafter "p13.5"). The presumptive role of p13.5, like p16 and p15, is in the regulation of the cell-cycle.

16. Document ID: US 5955306 A

L3: Entry 16 of 58

File: USPT

Sep 21, 1999

US-PAT-NO: 5955306
DOCUMENT-IDENTIFIER: US 5955306 A
TITLE: Genes encoding proteins that interact with the tub protein
DATE-ISSUED: September 21, 1999

US-CL-CURRENT: 435/69.1; 435/252.3, 435/254.11, 435/320.1, 435/325, 435/71.1, 536/23.5, 536/24.3, 536/24.31

APPL-NO: 8/ 897340
DATE FILED: July 21, 1997

PARENT-CASE:
RELATED APPLICATIONS This application is a continuation-in-part of U.S. Ser. No. 08/715,032, filed Sep. 17, 1996, now abandoned, the contents of which are incorporated herein by reference.

IN: Gimeno; Carlos J., Errada; Patrick R.

AB: The present invention relates to the discovery of novel genes encoding Tub interactor (TI) polypeptides. Therapeutics, diagnostics and screening assays based on these molecules are also disclosed.

17. Document ID: US 5948653 A

L3: Entry 17 of 58

File: USPT

Sep 7, 1999

US-PAT-NO: 5948653
DOCUMENT-IDENTIFIER: US 5948653 A
TITLE: Sequence alterations using homologous recombination
DATE-ISSUED: September 7, 1999

US-CL-CURRENT: 435/6; 435/470, 435/471, 435/490, 435/91.1,
435/DIG.37, 435/DIG.5, 435/DIG.6,
435/DIG.8, 530/350, 536/23.1

APPL-NO: 8/ 910367
DATE FILED: August 13, 1997

PARENT-CASE:
CROSS-REFERENCE TO RELATED APPLICATIONS This application
claims the benefit of U.S. application
Ser. No. 60/041,173, filed 21, Mar. 1997.

IN: Pati, Sushma, Zarling, David A.

AB: The invention relates to methods for targeting an exogenous polynucleotide or exogenous complementary polynucleotide pair to a predetermined endogenous DNA target sequence in a target cell by homologous pairing, particularly for altering an endogenous DNA sequence, such as a chromosomal DNA sequence, typically by targeted homologous recombination. In certain embodiments, the invention relates to methods for targeting an exogenous polynucleotide having a linked chemical substituent to a predetermined endogenous DNA sequence in a metabolically active target cell, generating a DNA sequence-specific targeting of one or more chemical substituents in an intact nucleus of a metabolically active target cell, generally for purposes of altering a predetermined endogenous DNA sequence in the cell. The invention also relates to compositions that contain exogenous targeting polynucleotides, complementary pairs of exogenous targeting polynucleotides, chemical substituents of such polynucleotides, and recombinase proteins used in the methods of the invention.

18. Document ID: US 5945339 A

L3: Entry 18 of 58

File: USPT

Aug 31, 1999

US-PAT-NO: 5945339
DOCUMENT-IDENTIFIER: US 5945339 A
TITLE: Methods to promote homologous recombination in eukaryotic cells and organisms
DATE-ISSUED: August 31, 1999

US-CL-CURRENT: 435/477; 435/483, 435/484

APPL-NO: 9/ 114637
DATE FILED: July 13, 1998

PARENT-CASE:
This application is a continuation of application Ser. No. 08/373,134, filed Jan. 17, 1995, now
U.S. Pat. No. 5,780,296.

IN: Holloman, William K., Kmiec, Eric B.

AB: The invention concerns genes encoding recombinases that can be used to promote homologous recombination in eukaryotic cells. The application teaches methods by which a recombinase of one species can be used to isolate a homologous recombinase of a different species and methods to identify the isolated homologs. Recombinases from *Ustilago maydis*, *Saccharomyces cerevisiae* and humans are specifically included in the invention. The invention encompasses the method of producing an isolated recombinase protein in a prokaryotic cell and recovering the product in an active form. The invention also encompasses a genetically engineered gene which encodes a non-naturally occurring recombinase that causes a greater rate of recombination than does the naturally occurring recombinase. The invention further encompasses the use of recombinase proteins and of recombinase genes to promote homologous recombination, including recombination between a host cell genome and a chimeric oligonucleotide, i.e., an oligonucleotide having both RNA and DNA bases.

19. Document ID: US 5919997 A

L3: Entry 19 of 58

File: USPT

Jul 6, 1999

US-PAT-NO: 5919997
DOCUMENT-IDENTIFIER: US 5919997 A
TITLE: Transgenic mice having modified cell-cycle regulation
DATE-ISSUED: July 6, 1999

US-CL-CURRENT: 800/18; 424/9.2, 435/320.1, 435/325, 435/455,
435/463, 435/467, 435/91.2, 800/22,
800/25, 800/3

APPL-NO: 8/ 627610
DATE FILED: April 4, 1996

PARENT-CASE:
RELATED APPLICATIONS This application is a continuation-in-part of U.S. Ser. No. 08/581,918 filed Jan. 2, 1996 which is a continuation-in-part of U.S. Ser. No. 08/497,214 filed Jun. 30, 1995, which is a continuation-in-part of U.S. Ser. No. 08/346,147 filed Nov. 29, 1994, which is a continuation-in-part of U.S. Ser. No. 08/306,511 filed Sep. 14, 1994, which is a continuation-in-part of U.S. Ser. No. 08/248,812 filed May 25, 1994, which is a continuation-in-part of U.S. Ser. No. 08/227,371 filed Apr. 14, 1994, which is a

continuation-in-part of U.S. Ser. No. 08/154,915 filed Nov. 18, 1993. The teachings of U.S. Ser.

Nos. 08/497,214, 08/346,147, 08/306,511, 08/248,812, 08/227,371 and 08/154,915 (hereinafter the "priority documents") are incorporated herein by reference.

IN: Beach; David H., Serrano; Manuel, DePinho; Ronald A.

AB: The present invention relates to transgenic mice in which the biological function of at least one cell cycle regulatory proteins of the INK4 family is altered.

20. Document ID: US 5912326 A

L3: Entry 20 of 58

File: USPT

Jun 15, 1999

US-PAT-NO: 5912326
DOCUMENT-IDENTIFIER: US 5912326 A
TITLE: Cerebellum-derived growth factors
DATE-ISSUED: June 15, 1999

US-CL-CURRENT: 530/399; 530/350

APPL-NO: 8/ 525864
DATE FILED: September 8, 1995

IN: Chang; Han

AB: The present invention relates to the discovery of a novel erbB receptor ligand, referred to hereinafter as "cdGF", which protein has apparently broad involvement in the formation and maintenance of ordered spatial arrangements of differentiated tissues in vertebrates, and can be used to generate and/or maintain an array of different vertebrate tissue both in vitro and in vivo.

21. Document ID: US 5910415 A

L3: Entry 21 of 58

File: USPT

Jun 8, 1999

US-PAT-NO: 5910415
DOCUMENT-IDENTIFIER: US 5910415 A
TITLE: Controlled modification of eukaryotic genomes
DATE-ISSUED: June 8, 1999

US-CL-CURRENT: 435/6; 435/320.1, 435/410, 536/23.1, 800/266, 800/267, 800/278

APPL-NO: 9/ 006232
DATE FILED: January 13, 1998

PARENT-CASE:

This is a Divisional of U.S. application Ser. No. 08/612,551 filed Mar. 8, 1996, now U.S. Pat.

No. 5,5744,336 which is a Divisional of U.S. application Ser. No. 08/010,997 filed Jan. 29, 1993, now U.S. Pat. No. 5,527,695.

IN: Hodges; Thomas K., Lyznik; Leszek A.

AB: A method of using a unique DNA construct for the creation of transgenic eukaryotic cells is described. The method allows a more precise and effective transformation procedure that targets the insertion of a DNA sequence into a predetermined DNA locus, while enabling the removal of any randomly inserted DNA sequences that occur as a by product of known transformation procedures.

22. Document ID: US 5885776 A

L3: Entry 22 of 58

File: USPT

Mar 23, 1999

US-PAT-NO: 5885776
DOCUMENT-IDENTIFIER: US 5885776 A
TITLE: Glaucoma compositions and therapeutic and diagnostic uses therefor
DATE-ISSUED: March 23, 1999

US-CL-CURRENT: 435/6

APPL-NO: 8/ 791347
DATE FILED: January 30, 1997

IN: Stone; Edwin M., Sheffield; Val C., Alward; Wallace L. M.

AB: Methods and compositions for treating glaucoma; and glaucoma diagnostics are disclosed.

23. Document ID: US 5882888 A

L3: Entry 23 of 58

File: USPT

Mar 16, 1999

US-PAT-NO: 5882888
DOCUMENT-IDENTIFIER: US 5882888 A
TITLE: DNA integration by transposition
DATE-ISSUED: March 16, 1999

US-CL-CURRENT: 435/69.1; 435/243, 435/252.31, 435/320.1, 435/473, 435/477, 435/478, 435/489, 435/91.4, 536/23.1, 536/24.2

APPL-NO: 8/ 875154
DATE FILED: July 17, 1997

FOREIGN-APPL-PRIORITY-DATA:
COUNTRY

APPL-NO

APPL-DATE
DK 0083/95
January 23, 1995
DK 0799/95
July 6, 1995

PCT-DATA:
APPL-NO
DATE-FILED
PUB-NO
PUB-DATE
371-DATE
102(E)-DATE
PCT/DK96/00038
Jan 23, 1996
WO96/23073
Aug 1, 1996
Jul 17, 1997
Jul 17, 1997

IN: J.o slashed.rgensen; Steen Troels

AB: Multicopy strains of gram-positive bacteria carrying multiple copies of a DNA sequence of interest may be constructed by use of a method involving introduction of a DNA construct comprising the DNA sequence of interest into the genome of the recipient cell by transposition and subsequent deletion of a marker gene used for selection of the cells having received the DNA construct by a resolution system. The multicopy strains are preferably free from a gene encoding an undesirable marker such as an antibiotic resistance marker.

24. Document ID: US 5874283 A
L3: Entry 24 of 58
File: USPT
Feb 23, 1999

US-PAT-NO: 5874283
DOCUMENT-IDENTIFIER: US 5874283 A
TITLE: Mammalian flap-specific endonuclease
DATE-ISSUED: February 23, 1999

US-CL-CURRENT: 435/252.3; 435/199, 435/252.33, 435/320.1, 435/69.1, 530/350, 536/23.2, 536/23.5

APPL-NO: 8/ 455968
DATE FILED: May 30, 1995

IN: Harrington; John Joseph, Hsieh; Chih-Lin, Lieber; Michael R.

AB: Compositions comprising human FEN-1(flap) endonucleases, nucleic acids encoding them, and methods for their use are provided.

25. Document ID: US 5849989 A
L3: Entry 25 of 58
File: USPT
Dec 15, 1998

US-PAT-NO: 5849989
DOCUMENT-IDENTIFIER: US 5849989 A
TITLE: Insulin promoter factor, and uses related thereto
DATE-ISSUED: December 15, 1998

US-CL-CURRENT: 800/9; 800/18

APPL-NO: 8/ 320148
DATE FILED: October 7, 1994

IN: Edlund; Thomas

AB: The present invention relates to the discovery in eukaryotic cells, particularly mammalian cells, of novel a transcriptional regulatory factor, referred to hereinafter as "Insulin Promoter Factor 1" or "Ipf1".

26. Document ID: US 5844079 A
L3: Entry 26 of 58
File: USPT
Dec 1, 1998

US-PAT-NO: 5844079
DOCUMENT-IDENTIFIER: US 5844079 A
TITLE: Vertebrate embryonic pattern-inducing proteins, and uses related thereto
DATE-ISSUED: December 1, 1998

US-CL-CURRENT: 530/350; 435/252.3, 435/320.1, 435/69.1, 435/7.1, 530/300, 536/23.1, 536/23.5

APPL-NO: 8/ 356060
DATE FILED: December 14, 1994

PARENT-CASE:
RELATED APPLICATIONS This application is a continuation-in-part of U.S. Ser. No. Ser. No. 08/176,427 filed Dec. 30, 1993 and entitled "Vertebrate Embryonic Pattern-Inducing Proteins and Uses Related Thereto", the teachings of which are incorporated herein by reference.

IN: Ingham; Philip W., McMahon; Andrew P., Tabin; Clifford J.

AB: The present invention concerns the discovery that proteins encoded by a family of vertebrate genes, termed here hedgehog-related genes, comprise morphogenic signals produced by embryonic patterning centers, and are involved in the formation of ordered spatial arrangements of differentiated tissues in vertebrates. The present invention makes available compositions and methods that can be utilized, for example to generate and/or maintain an array of different vertebrate tissue both in vitro and in vivo.

27. Document ID: US 5834202 A

L3: Entry 27 of 58

File: USPT

Nov 10, 1998

US-PAT-NO: 5834202
DOCUMENT-IDENTIFIER: US 5834202 A
TITLE: Methods for the isothermal amplification of nucleic acid molecules
DATE-ISSUED: November 10, 1998

US-CL-CURRENT: 435/6; 435/320.1, 435/91.1, 435/91.2, 536/23.1, 536/24.2, 536/24.33

APPL-NO: 8/ 906491
DATE FILED: August 5, 1997

PARENT-CASE:
CROSS-REFERENCE TO RELATED APPLICATIONS This application is a continuation-in-part of U.S. patent application Ser. No. 08/595,226 (filed Feb. 1, 1996, which issued on Mar. 31, 1998, as U.S. Pat. No. 5,733,733) which is a continuation-in-part of U.S. patent application Ser. No. 08/533,852 (filed Sep. 26, 1995, which issued on Mar. 25, 1997, as U.S. Pat. No. 5,614,389) which is a continuation-in-part of U.S. patent application Ser. No. 08/383,327 (filed Feb. 3, 1995, which issued on Jan. 7, 1997, as U.S. Pat. No. 5,591,609), which is a continuation-in-part of PCT Application No. PCT/US93/07309 (filed Aug. 4, 1993), which is a continuation-in-part of U.S. patent application Ser. No. 07/933,945, filed Aug. 24, 1992 (which application was abandoned in favor of continuation application U.S. patent application Ser. No. 08/136,405, filed Oct. 15, 1993, which issued on Oct. 11, 1994 as U.S. Pat. No. 5,354,668), which is a continuation-in-part of U.S. patent application Ser. No. 07/924,643, filed Aug. 4, 1992 (now abandoned).

IN: Auerbach; Jeffrey I.

AB: Methods for amplifying a nucleic acid molecule which employs a single primer, and in which the amplification is performed under isothermal conditions. The invention also includes kits containing reagents for conducting the method.

28. Document ID: US 5830461 A

L3: Entry 28 of 58

File: USPT

Nov 3, 1998

US-PAT-NO: 5830461
DOCUMENT-IDENTIFIER: US 5830461 A
TITLE: Methods for promoting wound healing and treating transplant-associated vasculopathy
DATE-ISSUED: November 3, 1998

US-CL-CURRENT: 424/94.4; 424/94.1, 435/189

APPL-NO: 8/ 745375
DATE FILED: November 8, 1996

PARENT-CASE:
CROSS-REFERENCE TO RELATED APPLICATIONS This application is a continuation-in-part of U.S. patent application Ser. No. 08/630,798, filed Apr. 10, 1996, and which is a continuation-in-part of U.S. patent application Ser. No. 08/265,046, filed Jun. 24, 1994, now U.S. Pat. No. 5,658,565, and a continuation-in-part of U.S. patent application Ser. No. 08/465,522, filed Jun. 5, 1995, which is a divisional of U.S. patent application Ser. No. 08/314,917, filed Sep. 28, 1994, now U.S. Pat. No. 5,468,630, which is a continuation of U.S. patent application Ser. No. 07/981,344, filed Nov. 25, 1992, now abandoned.

IN: Billiar; Timothy R.; Tzeng; Edith; Shears, II; Larry L.; Geller; David A.,
Edington; Howard David James

AB: The present invention provides a method of promoting the closure of a wound in a patient. This method involves transferring exogenous iNOS to the region of the wound whereby a product of iNOS is produced in the region of the wound to promote the closure of the wound.

29. Document ID: US 5807708 A

L3: Entry 29 of 58

File: USPT

Sep 15, 1998

US-PAT-NO: 5807708
DOCUMENT-IDENTIFIER: US 5807708 A
TITLE: Conservin nucleic acid molecules and compositions
DATE-ISSUED: September 15, 1998

US-CL-CURRENT: 435/69.1; 435/252.3, 435/254.11, 435/320.1, 435/325, 536/23.1, 536/23.5

APPL-NO: 8/ 688609
DATE FILED: July 30, 1996

IN: Falb; Dean A.; Gimeno; Carlos J.

AB: The present invention relates to the discovery of novel conservin genes and polypeptides. Therapeutics, diagnostics and screening assays based on these molecules are also disclosed.

30. Document ID: US 5800998 A

L3: Entry 30 of 58

File: USPT

Sep 1, 1998

US-PAT-NO: 5800998
DOCUMENT-IDENTIFIER: US 5800998 A
TITLE: Assays for diagnosing type II diabetes in a subject
DATE-ISSUED: September 1, 1998

US-CL-CURRENT: 435/6; 514/44, 536/23.1, 536/23.5

APPL-NO: 8/ 749431
DATE FILED: November 15, 1996

PARENT-CASE:
RELATED PATENT APPLICATIONS This patent application is a
continuation-in-part (CIP) application
of U.S. Ser. No. 08/748,229 filed Nov. 2, 1996 (abandoned).

IN: Glucksmann; M. Alexandra

AB: Assays for determining whether a subject has or is at risk for
developing type II
diabetes, which are based on detecting the presence or absence of
alterations in the hepatic
nuclear factor 1 (HNF-1) gene or protein of the subject are disclosed.

31. Document ID: US 5795726 A

L3: Entry 31 of 58

File: USPT

Aug 18, 1998

US-PAT-NO: 5795726
DOCUMENT-IDENTIFIER: US 5795726 A
TITLE: Methods for identifying compounds useful in treating type II
diabetes
DATE-ISSUED: August 18, 1998

US-CL-CURRENT: 435/7.21; 435/4, 435/6, 435/8, 536/23.5

APPL-NO: 8/ 782047
DATE FILED: January 10, 1997

PARENT-CASE:
RELATED PATENT APPLICATIONS The patent application is a
continuation-in-part (CIP) application of
U.S. Ser. No. 08/760,246 filed Dec. 4, 1996, which itself is a CIP of U.S.
Ser. No. 08/749,431
filed Nov. 15, 1996 which itself is a continuation-in-part of U.S. Ser. No.
08/748,229 filed Nov.
2, 1996 (abandoned).

IN: Glucksmann; M. Alexandra

AB: Methods for identifying compounds, which modulate the
bioactivity of human
hepatic nuclear factor-1 (HNF-1), and which are therefore useful in
treating type II
diabetes are disclosed.

32. Document ID: US 5795734 A

L3: Entry 32 of 58

File: USPT

Aug 18, 1998

US-PAT-NO: 5795734
DOCUMENT-IDENTIFIER: US 5795734 A
TITLE: EPH receptor ligands, and uses related thereto
DATE-ISSUED: August 18, 1998

US-CL-CURRENT: 435/69.1; 435/252.3, 435/320.1, 435/325, 435/7.1,
530/300, 530/350, 536/23.1,
536/23.5

APPL-NO: 8/ 455001
DATE FILED: May 31, 1995

PARENT-CASE:
REFERENCE TO RELATED APPLICATIONS This application in a
continuation-in-part of U.S. Ser. No.
08/393,462, filed Feb. 27, 1995 and entitled "EPH Receptor Ligands, and
Uses Related Thereto",
which is a continuation-in-part of U.S. Ser. No. 08/308,814, filed Sep. 19,
1994 and entitled
"EPH Receptor Ligands, and Uses Related Thereto". The disclosure of
U.S. Ser. No. 08/308,814 and
08/393,462 are incorporated by reference.

IN: Flanagan; John G., Cheng; Hwai-Jong

AB: The present invention relates to the discovery of a novel EPH
receptor ligand,
referred to hereinafter as "Elf-1", which protein has apparently broad
involvement in the
formation and maintenance of ordered spatial arrangements of
differentiated tissues in
vertebrates, and can be used to generate and/or maintain an array of
different vertebrate
tissue both in vitro and in vivo.

33. Document ID: US 5792833 A

L3: Entry 33 of 58

File: USPT

Aug 11, 1998

US-PAT-NO: 5792833
DOCUMENT-IDENTIFIER: US 5792833 A
TITLE: E2 binding proteins
DATE-ISSUED: August 11, 1998

US-CL-CURRENT: 530/350; 530/300

APPL-NO: 8/ 361806
DATE FILED: December 22, 1994

IN: Androphy; Elliot J., Breiding; David E.

AB: E2-BP polypeptides, nucleic acids encoding E2-BP
polypeptides, and uses thereof.

34. Document ID: US 5780296 A

L3: Entry 34 of 58

File: USPT

Jul 14, 1998

US-PAT-NO: 5780296
DOCUMENT-IDENTIFIER: US 5780296 A
TITLE: Compositions and methods to promote homologous recombination in eukaryotic cells and organisms
DATE-ISSUED: July 14, 1998
US-CL-CURRENT: 435/320.1; 536/23.2
APPL-NO: 8/ 373134
DATE FILED: January 17, 1995
IN: Holloman; William K., Kmiec; Eric B.

AB: The invention concerns genes encoding recombinases that can be used to promote homologous recombination in eukaryotic cells and expression vectors that can be used to transiently express recombinases in target cells. One embodiment of the invention encompasses genetically engineered nucleic acids that encode a non-naturally occurring recombinase that causes a greater rate of recombination than does the naturally occurring recombinase. Recombinases from *Ustilago maydis*, *Saccharomyces cerevisiae* are specifically included in the invention.

35. Document ID: US 5770384 A

L3: Entry 35 of 58

File: USPT

Jun 23, 1998

US-PAT-NO: 5770384
DOCUMENT-IDENTIFIER: US 5770384 A
TITLE: Method for determining compound interaction with E2 binding proteins
DATE-ISSUED: June 23, 1998
US-CL-CURRENT: 435/7.8; 435/5, 435/69.1, 435/69.7, 435/7.1, 435/7.93, 514/2, 530/300, 530/350, 536/23.72
APPL-NO: 8/ 612986
DATE FILED: March 6, 1996

PARENT-CASE:
This application is a divisional application of U.S. Ser. No. 08/361,806 filed on Dec. 22, 1994, pending. The contents of all of the aforementioned application are hereby incorporated by reference.

IN: Androphy; Elliot J., Breiding; David E.

AB: E2-BP polypeptides, nucleic acids encoding E2-BP polypeptides, and uses thereof.

36. Document ID: US 5763240 A

L3: Entry 36 of 58

File: USPT

Jun 9, 1998

US-PAT-NO: 5763240
DOCUMENT-IDENTIFIER: US 5763240 A
TITLE: In vivo homologous sequence targeting in eukaryotic cells
DATE-ISSUED: June 9, 1998
US-CL-CURRENT: 435/463; 435/6, 435/91.1, 435/91.4
APPL-NO: 8/ 275916
DATE FILED: July 14, 1994

PARENT-CASE:
This is a continuation of application Ser. No. 07/873,438 filed 24 Apr. 1992 now abandoned.

IN: Zarling; David A., Sena; Elissa P.

AB: The invention relates to methods for targeting an exogenous polynucleotide or exogenous complementary polynucleotide pair to a predetermined endogenous DNA target sequence in a eukaryotic cell by homologous pairing, particularly for altering an endogenous DNA sequence, such as a chromosomal DNA sequence, typically by targeted homologous recombination. In certain embodiments, the invention relates to methods for targeting an exogenous polynucleotide having a linked chemical substituent to a predetermined endogenous DNA sequence in a metabolically active eukaryotic cell, generating a DNA sequence-specific targeting of one or more chemical substituents in an intact nucleus of a metabolically active eukaryotic cell, generally for purposes of altering a predetermined endogenous DNA sequence in the cell. The invention also relates to compositions that contain exogenous targeting polynucleotides, complementary pairs of exogenous targeting polynucleotides, chemical substituents of such polynucleotides, and recombinase proteins used in the methods of the invention.

37. Document ID: US 5756671 A

L3: Entry 37 of 58

File: USPT

May 26, 1998

US-PAT-NO: 5756671
DOCUMENT-IDENTIFIER: US 5756671 A
TITLE: CDC37 cell-cycle regulatory protein, and uses related thereto
DATE-ISSUED: May 26, 1998

US-CL-CURRENT: 530/350; 530/300

APPL-NO: 8/ 625209
DATE FILED: April 1, 1996

PARENT-CASE:
RELATED APPLICATIONS This application is a continuation-in-part of U.S. Ser. No. 08/466,679 filed

Jun. 6, 1995, now abandoned, entitled "Cdc37 Cell-Cycle Regulatory Protein and Uses Related Thereto", which is a continuation-in-part of U.S. Ser. No. 08/253,155 filed Jun. 2, 1994, now U.S. Pat. No. 5,651,147, entitled "CDK4 Binding Proteins". The teachings of both U.S. Ser. Nos. 08/253,155 and 08/466,679 now abandoned are incorporated herein by reference.

IN: Gyuris; Jenö, Lamphere; Lou, Draetta; Giulio

AB: The present invention relates to the discovery in mammalian cells, particularly human cells, of a novel CDK-binding protein, referred to herein as "cdc37". As described herein, this protein functions to facilitate activation and accordingly functions in the modulation of cell-cycle progression, and therefore ultimately of cell growth and differentiation. Moreover, binding data indicated that cdc37 may function coordinately with other cell-cycle regulatory proteins, such as of cyclin-dependent kinases (CDKs), src, p53 and erk kinases.

38. Document ID: US 5744336 A

L3: Entry 38 of 58

File: USPT

Apr 28, 1998

US-PAT-NO: 5744336
DOCUMENT-IDENTIFIER: US 5744336 A
TITLE: DNA constructs for controlled transformation of eukaryotic cells
DATE-ISSUED: April 28, 1998

US-CL-CURRENT: 435/320.1; 536/23.1, 536/24.1, 536/24.2

APPL-NO: 8/ 612551
DATE FILED: March 8, 1996

PARENT-CASE:
This is a division of application Ser. No. 08/010,997, filed Jan. 29, 1993 now U.S. Pat. No. 5,527,695.

IN: Hodges; Thomas K., Lyznick; Leszek A.

AB: DNA constructs are provided for the creation of transgenic eukaryotic cells. These DNA constructs allow a more precise and effective transformation procedure by enabling the targeting of DNA sequences for insertion into a particular DNA locus, while enabling the removal of any randomly inserted DNA sequences that occur as a by product of known transformation procedures.

39. Document ID: US 5733733 A

L3: Entry 39 of 58

File: USPT

Mar 31, 1998

US-PAT-NO: 5733733
DOCUMENT-IDENTIFIER: US 5733733 A
TITLE: Methods for the isothermal amplification of nucleic acid molecules
DATE-ISSUED: March 31, 1998

US-CL-CURRENT: 435/6; 435/320.1, 435/5, 435/91.1, 435/91.2, 536/23.1, 536/24.3, 536/24.33

APPL-NO: 8/ 595226
DATE FILED: February 1, 1996

PARENT-CASE:
FIELD OF THE INVENTION The present invention is in the field of recombinant DNA technology. This invention is directed to a process for amplifying a nucleic acid molecule, and to the molecules employed and produced through this process. CROSS-REFERENCE TO RELATED APPLICATIONS This application is a continuation-in-part of U.S. patent application Ser. No. 08/533,852 (filed Sep. 26, 1995, now U.S. Pat. No. 5,614,389) which is a continuation-in-part of U.S. patent application Ser. No. 08/383,327 (filed Feb. 3, 1995) now U.S. Pat. No. 5,591,609, which is a continuation-in-part of PCT Application No. PCT/US93/07309 (filed Aug. 4, 1993), which is a continuation-in-part of U.S. patent application Ser. No. 07/933,945, filed Aug. 24, 1992 (which application was abandoned in favor of continuation application U.S. patent application Ser. No. 08/136,405, filed Oct. 15, 1993, which issued on Oct. 11, 1994 as U.S. Pat. No. 5,354,668), which is a continuation-in-part of U.S. patent application Ser. No. 07/924,643, filed Aug. 4, 1992 (now abandoned).

IN: Auerbach; Jeffrey I.

AB: Methods for amplifying a nucleic acid molecule which employs a single primer, and in which the amplification is performed under isothermal conditions. The invention also includes kits containing reagents for conducting the method.

40. Document ID: US 5635381 A

L3: Entry 40 of 58

File: USPT

Jun 3, 1997

US-PAT-NO: 5635381
DOCUMENT-IDENTIFIER: US 5635381 A
TITLE: Agrobacterium bacteria capable of site-specific recombination
DATE-ISSUED: June 3, 1997

US-CL-CURRENT: 800/294; 435/199, 435/252.2, 435/252.3, 435/320.1, 435/419, 435/477, 435/71.2, 536/23.72

APPL-NO: 8/ 290933
DATE FILED: January 20, 1995

FOREIGN-APPL-PRIORITY-DATA:
COUNTRY
APPL-NO

NL
APPL-DATE
922005582
February 26, 1992

PCT-DATA:
APPL-NO
DATE-FILED
PUB-NO
PUB-DATE
371-DATE
102(E)-DATE
PCT/EP93/00463
Feb 25, 1993
WO93/17116
Sep 2, 1993
Jan 20, 1995
Jan 20, 1995

IN: Hooykaas; Paul J. J., Mozo; Teresa

AB: The invention provides Agrobacterium strains capable of producing a site-specific recombinase capable of effecting site-specific recombination of a first and a second recombination site in Agrobacterium strains, when present therein, comprising a structural DNA sequence encoding said recombinase and a DNA sequence capable of controlling expression in Agrobacterium strains. The invention also provides methods for using the strains to transform plant cells.

41. Document ID: US 5631237 A

L3: Entry 41 of 58
File: USPT
May 20, 1997

US-PAT-NO: 5631237
DOCUMENT-IDENTIFIER: US 5631237 A
TITLE: Method for producing in vivo delivery of therapeutic agents via liposomes
DATE-ISSUED: May 20, 1997
US-CL-CURRENT: 514/44; 264/4.1, 264/4.3, 264/4.6, 424/417, 424/450, 428/402.2

APPL-NO: 8/ 241372
DATE FILED: May 10, 1994

PARENT-CASE:
CROSS-REFERENCE TO RELATED APPLICATIONS This application is a continuation-in-part of Ser. No. 07/995,022, filed Dec. 22, 1992 (now abandoned).

IN: Dzau; Victor J., Kaneda; Yasufumi

AB: Methods and compositions are provided for intracellular transfer of a wide variety of agents, by using Sendai virus comprising liposomes having various compositions in the liposome lumen. A preferred method for preparing the liposomes provides for enhanced levels of luminal concentrations, as well as incorporation of high molecular weight

molecules. The method comprises fusing liposomes, where one liposome comprises the Sendai virus proteins and the other liposome comprises the luminal composition. The subject methods find particular application with intranuclear transfer of nucleic acids, more particularly with cells of the vasculature.

42. Document ID: US 5614389 A

L3: Entry 42 of 58
File: USPT
Mar 25, 1997

US-PAT-NO: 5614389
DOCUMENT-IDENTIFIER: US 5614389 A
TITLE: Methods for the isothermal amplification of nucleic acid molecules
DATE-ISSUED: March 25, 1997

US-CL-CURRENT: 435/91.2; 435/6, 435/91.1

APPL-NO: 8/ 533852
DATE FILED: September 26, 1995

PARENT-CASE:
CROSS-REFERENCE TO RELATED APPLICATIONS This application is a continuation-in-part of U.S. patent application Ser. No. 08/383,327 (filed Feb. 3, 1995), which is a continuation-in-part of PCT Application No. PCT/US93/07309 (filed Aug. 4, 1993), which is a continuation-in-part of U.S. patent application Ser. No. 07/933,945, filed Aug. 24, 1992 (which application was abandoned in favor of continuation application U.S. patent application Ser. No. 08/136,405, filed Oct. 15, 1993, which issued on Oct. 11, 1994 as U.S. Pat. No. 5,354,668, U.S. patent application Ser. No. 07/933,445, which is a continuation-in-part of U.S. patent application Ser. No. 07/924,643, filed Aug. 4, 1992 (now abandoned).

IN: Auerbach; Jeffrey I.

AB: Methods for amplifying a nucleic acid molecule which employs a single primer, and in which the amplification is performed under isothermal conditions. The invention also includes kits containing reagents for conducting the method.

43. Document ID: US 5591609 A

L3: Entry 43 of 58
File: USPT
Jan 7, 1997

US-PAT-NO: 5591609
DOCUMENT-IDENTIFIER: US 5591609 A
TITLE: Methods for the isothermal amplification of nucleic acid molecules
DATE-ISSUED: January 7, 1997

US-CL-CURRENT: 435/91.2; 435/6, 435/91.1, 435/91.5

APPL-NO: 8/ 383327
DATE FILED: February 3, 1995

PARENT-CASE:

CROSS-REFERENCE TO RELATED APPLICATIONS This application is a continuation-in-part of PCT

Application No. PCT/US93/07309 (filed Aug. 4, 1993), which is a continuation-in-part of U.S.

patent application Ser. No. 07/933,945, filed Aug. 24, 1992 (which application was abandoned in

favor of continuation application U.S. patent application Ser. No. 08/136,405, filed Oct. 15,

1993, which issued on Oct. 11, 1994 as U.S. Pat. No. 5,354,668) and U.S. patent application Ser.

No. 07/933,945 is a continuation-in-part of U.S. patent application Ser. No. 07/924,643, filed

Aug. 4, 1992 (now abandoned).

IN: Auerbach; Jeffrey I.

AB: Methods for amplifying a nucleic acid molecule which employs a single primer, and in which the amplification is performed under isothermal conditions. The invention also

includes kits containing reagents for conducting the method.

44. Document ID: US 5571688 A

L3: Entry 44 of 58

File: USPT

Nov 5, 1996

US-PAT-NO: 5571688

DOCUMENT-IDENTIFIER: US 5571688 A

TITLE: Method of detecting gene expression

DATE-ISSUED: November 5, 1996

US-CL-CURRENT: 435/29; 435/34, 435/6

APPL-NO: 8/ 396415

DATE FILED: February 27, 1995

PARENT-CASE:

CROSS-REFERENCE TO OTHER APPLICATIONS This patent application is a continuation-in-part of U.S.

patent application Ser. No. 08/127,905, filed Sep. 28, 1993, pending and entitled Selection of

Bacterial Genes Induced in Host Tissue which is a continuation-in-part of U.S. patent application

Ser. No. 08/058,299, filed May 6, 1993, now U.S. Pat. No. 5,434,065 and entitled In Vivo

Selection of Microbial Virulence Genes.

IN: Mekalanos; John J., Camilli; Andrew

AB: A reporter system relating to in vivo expression technology was devised to aid in the identification and study of genes that display temporal or spatial patterns of

expression during infection of host tissues. The method of this invention comprises

constructing a strain or pool of strains of a microorganism which contains an artificial

cointegrate comprising a reporter gene flanked by direct repeats of sequences to which a

resolvase enzyme binds, thus catalyzing excision of the reporter gene, and further contains

a coding sequence under the control of a promoter sequence which

encodes transcripts, the

expression of which are easily monitored in vitro and which result in a permanent genetic

change, excision of the reporter gene, that is heritable and easily detectable subsequent to

induction of the synthetic operon.

45. Document ID: US 5527695 A

L3: Entry 45 of 58

File: USPT

Jun 18, 1996

US-PAT-NO: 5527695

DOCUMENT-IDENTIFIER: US 5527695 A

TITLE: Controlled modification of eukaryotic genomes

DATE-ISSUED: June 18, 1996

US-CL-CURRENT: 800/291; 435/320.1

APPL-NO: 8/ 010997

DATE FILED: January 29, 1993

IN: Hodges; Thomas K., Lyznik; Leszek A.

AB: DNA constructs are provided for the creation of transgenic eukaryotic cells.

These DNA constructs allow a more precise and effective transformation procedure by enabling

the targeting of DNA sequences for insertion into a particular DNA locus, while enabling the

removal of any randomly inserted DNA sequences that occur as a by product of known

transformation procedures.

46. Document ID: US 5512452 A

L3: Entry 46 of 58

File: USPT

Apr 30, 1996

US-PAT-NO: 5512452

DOCUMENT-IDENTIFIER: US 5512452 A

TITLE: Selection of bacterial genes induced in host tissues

DATE-ISSUED: April 30, 1996

US-CL-CURRENT: 435/25; 435/6

APPL-NO: 8/ 127905

DATE FILED: September 28, 1993

PARENT-CASE:

CROSS-REFERENCE TO OTHER APPLICATIONS This patent application is a continuation-in-part of U.S.

patent application No. 08/058299, filed May 6, 1993, U.S. Pat. No. 5,434,065, and entitled In

Vivo Selection of Microbial Virulence Genes.

IN: Mekalanos; John J., Camilli; Andrew

AB: A reporter system relating to in vivo expression technology was devised to aid in the identification and study of genes that display temporal or spatial patterns of expression during infection of host tissues. The method of this invention comprises integrating a site-specific DNA recombinase expression vector, and a reporter gene that is permanently removable by the recombinase, by way of homologous recombination into a microorganism's chromosome and inducing the expression of a synthetic operon which encodes transcripts, the expression of which are easily monitored in vitro and which result in a permanent genetic change, excision of the reporter gene, that is heritable and easily detectable subsequent to induction of the synthetic operon.

47. Document ID: US 5354668 A

L3: Entry 47 of 58

File: USPT

Oct 11, 1994

US-PAT-NO: 5354668
DOCUMENT-IDENTIFIER: US 5354668 A
TITLE: Methods for the isothermal amplification of nucleic acid molecules
DATE-ISSUED: October 11, 1994

US-CL-CURRENT: 435/91.1; 435/6

APPL-NO: 8/ 136405
DATE FILED: October 15, 1993

PARENT-CASE:
CROSS-REFERENCE TO RELATED APPLICATIONS This application is a continuation of U.S. patent application Ser. No. 07/933,945, filed Aug. 24, 1992, now abandoned, which application was a continuation-in-part of U.S. patent application Ser. No. 07/924,643, filed Aug. 4, 1992.

IN: Auerbach; Jeffrey I.

AB: Methods for amplifying a nucleic acid molecule which employs a single primer, and in which the amplification is performed under isothermal conditions. The invention also includes kits containing reagents for conducting the method.

48. Document ID: US 5102797 A

L3: Entry 48 of 58

File: USPT

Apr 7, 1992

US-PAT-NO: 5102797
DOCUMENT-IDENTIFIER: US 5102797 A
TITLE: Introduction of heterologous genes into bacteria using transposon flanked expression cassette and a binary vector system

DATE-ISSUED: April 7, 1992

US-CL-CURRENT: 435/473; 435/320.1

APPL-NO: 7/ 357492
DATE FILED: May 26, 1989

IN: Tucker; William T.; Gutterson; Neal I.

AB: This invention relates to a new method for inserting heterologous genes into the genome of a bacteria using a combined plasmid. The combined plasmid provides a cis complementation of transposase genes and transposable elements. The method involves the homologous recombination of a carrier plasmid and a functions plasmid to form the combined plasmid. The carrier plasmid contains a transposable element which flanks a generic expression cassette. The functions plasmid comprises transposase genes which complement the transposable element on the carrier plasmid. The combined plasmid is then transferred to a recipient and the recipient is monitored for integration of the generic expression cassette into the genome. The combined plasmid is preferably created by an in vivo homologous recombination of the carrier and functions plasmids.

49. Document ID: JP 11225785 A

L3: Entry 49 of 58

File: JPAB

Aug 24, 1999

PUB-NO: JP411225785A
DOCUMENT-IDENTIFIER: JP 11225785 A
TITLE: OPTIMIZATION OF CELL FOR ENDOGENOUS GENE ACTIVATION

PUBN-DATE: August 24, 1999

INT-CL (IPC): C12N 15/09; C12N 5/10; C12Q 1/68

APPL-NO: JP10342234
APPL-DATE: December 1, 1998

IN: HONOLD, KONRAD, HOLTSCHKE, THOMAS, STERN, ANNE

AB: PROBLEM TO BE SOLVED: To optimize the expression of a nucleic acid in cells by transfecting cells with a vector comprising a heteroexpression control sequence or the like, positive selection marker gene, site-specific recombinase target sequence and sequence capable of homologous recombination, followed by culturing the resultant cells., SOLUTION: The expression of a nucleic acid sequence endogenous in eukaryocytes is optimized by the following procedure: cells are transfected with a 1st vector comprising a 1st heteroexpression control sequence and a sequence of a 1st amplification gene or the like, positive selection marker gene, at least two target sequences of a site-specific recombinase, adjacent to the above sequences, and such a DNA sequence

as to be adjacent to
the above sequences and homologous with the nucleic acid portion in the
genome of the cells
so as to be capable of homologous recombination; the resulting
transfected cells are
cultured under such conditions as to cause the homologous recombination
of the above vector,
and the resulting cells are isolated., COPYRIGHT: (C)1999,JPO

50. Document ID: US 5780296 A

L3: Entry 50 of 58

File: EPAB

Jul 14, 1998

PUB-NO: US005780296A
DOCUMENT-IDENTIFIER: US 5780296 A
TITLE: Compositions and methods to promote homologous recombination
in eukaryotic cells and
organisms

PUBN-DATE: July 14, 1998

INT-CL (IPC): C12N 15/63
EUR-CL (EPC): C12N009/00

APPL-NO: US37313495
APPL-DATE: January 17, 1995
PRIORITY-DATA: US37313495A (January 17, 1995)

IN: HOLLOMAN, WILLIAM K, KMEIC, ERIC B

AB: The invention concerns genes encoding recombinases that can
be used to promote
homologous recombination in eukaryotic cells and expression vectors that
can be used to
transiently express recombinases in target cells. One embodiment of the
invention
encompasses genetically engineered nucleic acids that encode a
non-naturally occurring
recombinase that causes a greater rate of recombination than does the
naturally occurring
recombinase. Recombinases from *Ustilago maydis*, *Saccharomyces*
cerevisiae are specifically
included in the invention.

51. Document ID: WO 9622364 A1

L3: Entry 51 of 58

File: EPAB

Jul 25, 1996

PUB-NO: WO009622364A1
DOCUMENT-IDENTIFIER: WO 9622364 A1
TITLE: COMPOSITIONS AND METHODS TO PROMOTE
HOMOLOGOUS RECOMBINATION IN EUKARYOTIC CELLS AND
ORGANISMS

PUBN-DATE: July 25, 1996

INT-CL (IPC): C12N 9/00; C12N 9/22
EUR-CL (EPC): C12N009/00

APPL-NO: US09600265
APPL-DATE: January 16, 1996
PRIORITY-DATA: US37313495A (January 17, 1995)

IN: HOLLOMAN, WILLIAM K, KMEIC, ERIC B

AB: The invention concerns genes encoding recombinases that can
be used to promote
homologous recombination in eukaryotic cells. The application teaches
methods by which a
recombinase of one species can be used to isolate a homologous
recombinase of a different
species and methods to identify the isolated homologs. Recombinases
from *Ustilago maydis* and
Saccharomyces cerevisiae are specifically included in the invention. The
invention
encompasses the method of producing an isolated recombinase protein in
a prokaryotic cell
and recovering the product in an active form. The invention also
encompasses a genetically
engineered gene which encodes a non-naturally occurring recombinase
that causes a greater
rate of recombination than does the naturally occurring recombinase. The
invention further
encompasses the use of recombinase proteins and of recombinase genes
to promote homologous
recombination, including recombination between a host cell genome and a
chimeric
oligonucleotide, i.e., an oligonucleotide having both RNA and DNA
bases.

52. Document ID: US 5512452 A

L3: Entry 52 of 58

File: EPAB

Apr 30, 1996

PUB-NO: US005512452A
DOCUMENT-IDENTIFIER: US 5512452 A
TITLE: Selection of bacterial genes induced in host tissues

PUBN-DATE: April 30, 1996

INT-CL (IPC): C12Q 1/02; C12N 15/00
EUR-CL (EPC): C07K014/255; C12N015/10, C12N015/52, C12N015/62
, C12N015/90, C12Q001/68

APPL-NO: US12790593
APPL-DATE: September 28, 1993
PRIORITY-DATA: US12790593A (September 28, 1993)

IN: MEKALANOS, JOHN J, CAMILLI, ANDREW

AB: A reporter system relating to in vivo expression technology was
devised to aid in
the identification and study of genes that display temporal or spatial
patterns of
expression during infection of host tissues. The method of this invention
comprises
integrating a site-specific DNA recombinase expression vector, and a
reporter gene that is
permanently removable by the recombinase, by way of homologous
recombination into a
microorganism's chromosome and inducing the expression of a synthetic

operon which encodes transcripts, the expression of which are easily monitored in vitro and which result in a permanent genetic change, excision of the reporter gene, that is heritable and easily detectable subsequent to induction of the synthetic operon.

53. Document ID: AU 9919135 A, WO 9937755 A2
L3: Entry 53 of 58

File: DWPI

Aug 9, 1999

DERWENT-ACC-NO: 1999-458689
DERWENT-WEEK: 200001
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TITLE: New compositions and methods for targeting sequence modifications in related family genes

PRIORITY-DATA:
1997US-0070734

December 11, 1997

PATENT-FAMILY:
PUB-NO

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
AU 9919135 A	August 9, 1999	N/A	000	C12N015/00
WO 9937755 A2	July 29, 1999	E	047	C12N015/00

APPLICATION-DATA:
PUB-NO

PUB-NO	APPL-DATE	APPL-NO	APPL-DESCRIPTOR
AU 9919135A	December 11, 1998	1999AU-0019135	N/A
AU 9919135A	N/A	WO 9937755	Based on
WO 9937755A2	December 11, 1998	1998WO-US26498	N/A

INT-CL (IPC): C12N 15/00

IN: LEHMAN, C W, PATI, S, ZARLING, D, ZENG, H

AB: NOVELTY - A composition is new comprising at least one recombinase and at least two single-stranded targeting polynucleotides (I) which are substantially complementary to

each other and each having a consensus homology clamp for a gene family i.e. a homology motif tag (HMT)., DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following., (1) a method (A) for targeting a sequence modification in at least one member of a consensus family of genes in a cell by homologous recombination. The method involves introducing into at least one cell at least one recombinase and (I)., (2) a method (B) of making a non-human organism with a targeted sequence modification in at least one member of a gene family by introducing into a cell at least one recombinase and (I). The animal formed has at least one modification in at least one member of a consensus family of genes., (3) a method (C) of isolating a member of a gene family comprising a protein consensus sequence. The method involves., (a) adding the recombinase and (I) to a complex mixture of nucleic acids where the targeting polynucleotides comprise a purification tag; and, (b) isolating the member using the purification tag; and, (4) a non-human organism containing a sequence modification in an endogenous consensus functional domain of a gene member of a gene family., USE - The composition is useful in kit form which include the composition as libraries or pools of degenerate cssDNA probes along with other reagents such as recombinase etc. The methods and compositions are used for inactivation of a gene family gene i.e. exogenous targeting polynucleotides can be used to inactivate, decrease or alter the biological activity of one or more genes in a cell (or transgenic nonhuman animal or plant). This is useful in the generation of animal models of disease, or in the elucidation of gene function and activity. Alternatively, the biological activity of the wild-type gene may be either decreased or the wild-type activity altered to mimic disease states. This includes genetic manipulation of non-coding gene sequences that affect the transcription of genes, including promoter, repressors, enhancers and transcriptional activating sequences., The compositions are useful in identifying new members of gene families which may be useful in functional genomic studies as well as in identification of new drug targets. HMTs used in homologous recombination methods can generate animals that have a wide variety of mutations in a wide variety of related genes, potentially resulting in a wide variety of phenotypes including those related to disease states. This may also be done on a cellular level to identify genes involved in cellular phenotypes i.e. target identification., ADVANTAGE - This invention provides compositions and methods for the evaluation and characterization of individual and sets of genes in disease states., Traditionally, exogenous sequences transferred into eukaryotic cells underwent homologous recombination with homologous endogenous sequences only at very low frequencies. Hence they were recombined inefficiently and large numbers of cells were needed to be transfected, selected and screened in order to generate a correctly targeted homologous recombinant. Several proteins or purified extracts having the property of promoting homologous recombination (recombinase activity) have recently been identified and the frequency of homologous recombination is enhanced by the presence of these recombinase activities. Such recent advances have resulted in techniques allowing enhanced homologous recombination (EHR)., Relaxing the amount of sequence identity

needed for homologous recombination allows greater flexibility to target related genes for creating transgenic animals and cells containing modifications in gene family consensus sequences.

54. Document ID: EP 977771 A1, WO 9842727 A1, AU 9865620 A, US 5948653 A
L3: Entry 54 of 58

File: DWPI

Feb 9, 2000

DERWENT-ACC-NO: 1998-542274
DERWENT-WEEK: 200012
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TITLE: Modification of target polynucleotide sequences - by homologous recombination using recombinase and at least 2 single stranded polynucleotides complementary to each other, used for, e.g. correcting diseased alleles in cystic fibrosis

PRIORITY-DATA:

1997US-0910367

August 13, 1997

1997US-0041173

March 21, 1997

PATENT-FAMILY:

PUB-NO

PUB-DATE

LANGUAGE

PAGES

MAIN-IPC

EP 977771 A1

February 9, 2000

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C07H021/04

WO 9842727 A1

October 1, 1998

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C07H021/04

AU 9865620 A

October 20, 1998

N/A

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C07H021/04

US 5948653 A

September 7, 1999

N/A

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C07H021/04

APPLICATION-DATA:

PUB-NO

APPL-DATE

APPL-NO

APPL-DESCRIPTOR

EP 977771 A1

March 16, 1998

1998EP-0911735

N/A

EP 977771 A1

March 16, 1998

1998WO-US05223

N/A

EP 977771 A1

N/A

WO 9842727

Based on

WO 9842727 A1

March 16, 1998

1998WO-US05223

N/A

AU 9865620 A

March 16, 1998

1998AU-0065620

N/A

AU 9865620 A

N/A

WO 9842727

Based on

US 5948653 A

March 21, 1997

1997US-0041173

Provisional

US 5948653 A

August 13, 1997

1997US-0910367

N/A

INT-CL (IPC): C07H 21/04; C07K 14/00; C12N 15/00; C12P 19/34

IN: PATI, S, ZARLING, D A

AB: The following are claimed: (1) preparation of a targeted sequence modification (TSM) in a preselected target DNA sequence in a eukaryotic zygote by homologous recombination, comprising introducing into at least 1 eukaryotic zygote at least 1 recombinase and at least 2 single-stranded (ss) targeting polynucleotides (PNs) that are complementary to each other, and each having a homology clamp (HC) corresponding to or is complementary to a preselected target DNA sequence; (2) preparation of TSM in a preselected target DNA sequence in a cell by homologous recombination which contains an insertion, carried out as in (1), but where PNs also each have an internal HC; (3) a method for targeting and altering, by homologous recombination, a pre-selected target NA sequence in an extrachromosomal sequence (ExS) of a prokaryotic cell, comprising: (a) adding to the extrachromosomal sequence materials as in (1); (b) removing the recombinase, and (c) introducing the altered element into a prokaryotic cell; (4) a method of generating a pool of variant NA sequences of a pre-selected target NA sequence in ExS, comprising adding to ExS at least 1 recombinase and pairs of ss targeting PNs which are complementary to each other and each comprising HC corresponding to or being complementary to a preselected target NA sequence, the pairs comprising a library of mismatches between the targeting PN and the target NA sequence, to form a library of altered ExS's; (5) a method of generating a cellular library comprising variant NA sequences of a pre-selected target NA sequence, comprising introducing into a population of target cells materials as in (4), and (6) a method similar to (5) comprising: (a) adding to ExS materials as in (4), to form altered ExS's; (b) as in (3b), and (c) introducing the altered sequences into a population of a target cells to form the library of variant NA sequences., USE - The method of (1) may be used for targeting and altering, by homologous recombination, a pre-selected target nucleic acid (NA) sequence (claimed). The methods can provide for the efficient

and specific modification of targeted PNs. The methods can be used, e.g. to target chemical substituents in a sequence-specific manner in vivo, to correct or to generate genetic mutations in endogenous DNA sequences by homologous recombination and/or gene conversion, to produce homologously targeted transgenic organisms, including animals and plants at high efficiency, and in other application, e.g. targeted drug delivery, based on in vivo homologous pairing.

The methods can be used for correcting disease alleles involved in producing human genetic diseases, such as inherited genetic diseases (e.g. cystic fibrosis) and neoplasia (e.g. neoplasms induced by somatic mutation of an oncogene or tumour suppressor gene, such as p53) or acquired diseases, particularly parasitic or viral diseases, such as human hepatitis B virus (HBV) infection. The following are claimed: (1) preparation of a targeted sequence modification (TSM) in a preselected target DNA sequence in a eukaryotic zygote by homologous recombination, comprising introducing into at least 1 eukaryotic zygote at least 1 recombinase and at least 2 single-stranded (ss) targeting polynucleotides (PNs) that are complementary to each other, and each having a homology clamp (HC) corresponding to or is complementary to a preselected target DNA sequence; (2) preparation of TSM in a preselected target DNA sequence in a cell by homologous recombination which contains an insertion, carried out as in (1), but where PNs also each have an internal HC; (3) a method for targeting and altering, by homologous recombination, a pre-selected target NA sequence in an extrachromosomal sequence (ExS) of a prokaryotic cell, comprising: (a) adding to the extrachromosomal sequence materials as in (1); (b) removing the recombinase, and (c) introducing the altered element into a prokaryotic cell; (4) a method of generating a pool of variant NA sequences of a pre-selected target NA sequence in ExS, comprising adding to ExS at least 1 recombinase and pairs of ss targeting PNs which are complementary to each other and each comprising HC corresponding to or being complementary to a preselected target NA sequence, the pairs comprising a library of mismatches between the targeting PN and the target NA sequence, to form a library of altered ExS's; (5) a method of generating a cellular library comprising variant NA sequences of a pre-selected target NA sequence, comprising introducing into a population of target cells materials as in (4), and (6) a method similar to (5) comprising: (a) adding to ExS materials as in (4), to form altered ExS's; (b) as in (3b), and (c) introducing the altered sequences into a population of target cells to form the library of variant NA sequences. USE - The method of (1) may be used for targeting and altering, by homologous recombination, a pre-selected target nucleic acid (NA) sequence (claimed). The methods can provide for the efficient and specific modification of targeted PNs. The methods can be used, e.g. to target chemical substituents in a sequence-specific manner in vivo, to correct or to generate genetic mutations in endogenous DNA sequences by homologous recombination and/or gene conversion, to produce homologously targeted transgenic organisms, including animals and plants at high efficiency, and in other application, e.g. targeted drug delivery, based on in vivo homologous pairing.

The methods can be used for correcting disease alleles involved in

producing human genetic diseases, such as inherited genetic diseases (e.g. cystic fibrosis) and neoplasia (e.g. neoplasms induced by somatic mutation of an oncogene or tumour suppressor gene, such as p53) or acquired diseases, particularly parasitic or viral diseases, such as human hepatitis B virus (HBV) infection.

55. Document ID: US 5945339 A, WO 9622364 A1, AU 9646960 A, US 5780296 A, EP 873402 A1
L3: Entry 55 of 58

File: DWPI

Aug 31, 1999

DERWENT-ACC-NO: 1996-354521
DERWENT-WEEK: 199942
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TITLE: Isolated recombinase enzyme and gene - obtd. from *Ustilago maydis*, used to promote homologous recombination in eukaryotic cells

PRIORITY-DATA:
1995US-0373134

January 17, 1995

1998US-0114637

July 13, 1998

PATENT-FAMILY:
PUB-NO

PUB-DATE

LANGUAGE
PAGES

MAIN-IPC

US 5945339 A

August 31, 1999

N/A

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C12N015/64

WO 9622364 A1

July 25, 1996

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C12N009/00

AU 9646960 A

August 7, 1996

N/A

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C12N009/00

US 5780296 A

July 14, 1998

N/A

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C12N015/63

EP 873402 A1

October 28, 1998

E

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C12N009/00

APPLICATION-DATA:
PUB-NO

APPL-DATE

APPL-NO

APPL-DESCRIPTOR

US 5945339A

January 17, 1995

1995US-0373134
Cont of
US 5945339A
July 13, 1998
1998US-0114637
N/A
US 5945339A
N/A
US 5780296
Cont of
WO 9622364A1
January 16, 1996
1996WO-US00265
N/A
AU 9646960A
January 16, 1996
1996AU-0046960
N/A
AU 9646960A
N/A
WO 9622364
Based on
US 5780296A
January 17, 1995
1995US-0373134
N/A
EP 873402A1
January 16, 1996
1996EP-0902629
N/A
EP 873402A1
January 16, 1996
1996WO-US00265
N/A
EP 873402A1
N/A
WO 9622364
Based on
INT-CL (IPC): C12N 9/00; C12N 9/22; C12N 15/63; C12N 15/64
IN: HOLLOMAN, W K, KMIEC, E B
AB: Novel isolated protein (A): (a) is an ATPase having an apparent mol.wt. by SDS-PAGE of greater than 70 kD; (b) catalyses the formation of complementary or identical strand pairings of polydeoxynucleic acids (PDAs); (c) promotes homologous recombination (HR) in a eukaryote; and (d) has a sequence contg. the tetrapeptide (I): (Ser/Thr)-Pro-Xaa-(Arg /Lys) (I), Xaa = any amino acid., USE - The prods. and methods can be used to promote HR in cells for, e.g. making specific genetic alterations in cells to produce a recombinant protein, introducing specific alterations in embryonic stem cells or ova to be used in the construction of transgenic animals, modifying in vitro explanted tissue stem cells, e.g. haematopoietic stem cells, which can then be continued in culture or reimplanted into a non-human host to produce a specific prod. or reimplanted into a human subject in need of gene therapy for a medical condition., Novel isolated protein (A): (a) is an ATPase having an apparent mol.wt. by SDS-PAGE of greater than 70 kD; (b) catalyses the formation of complementary or identical strand pairings of polydeoxynucleic acids (PDAs); (c) promotes homologous recombination (HR) in a eukaryote; and (d) has a sequence contg. the tetrapeptide (I): (Ser/Thr)-Pro-Xaa-(Arg /Lys) (I), Xaa = any amino acid., USE - The prods. and methods can be used to promote HR in cells for, e.g. making specific genetic alterations in cells to produce a recombinant protein, introducing specific alterations in

embryonic stem cells or ova to be used in the construction of transgenic animals, modifying in vitro explanted tissue stem cells, e.g. haematopoietic stem cells, which can then be continued in culture or reimplanted into a non-human host to produce a specific prod. or reimplanted into a human subject in need of gene therapy for a medical condition., Novel isolated protein (A): (a) is an ATPase having an apparent mol.wt. by SDS-PAGE of greater than 70 kD; (b) catalyses the formation of complementary or identical strand pairings of polydeoxynucleic acids (PDAs); (c) promotes homologous recombination (HR) in a eukaryote; and (d) has a sequence contg. the tetrapeptide (I): (Ser/Thr)-Pro-Xaa-(Arg /Lys) (I), Xaa = any amino acid., USE - The prods. and methods can be used to promote HR in cells for, e.g. making specific genetic alterations in cells to produce a recombinant protein, introducing specific alterations in embryonic stem cells or ova to be used in the construction of transgenic animals, modifying in vitro explanted tissue stem cells, e.g. haematopoietic stem cells, which can then be continued in culture or reimplanted into a non-human host to produce a specific prod. or reimplanted into a human subject in need of gene therapy for a medical condition.

56. Document ID: US 5910415 A, WO 9417176 A1, EP 686191 A1, US 5527695 A, US 5744336 A
L3: Entry 56 of 58

File: DWPI

Jun 8, 1999

DERWENT-ACC-NO: 1994-264090
DERWENT-WEEK: 199930
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TITLE: DNA constructs - for creating transgenic eukaryotic cells

PRIORITY-DATA:
1993US-0010997

January 29, 1993

1996US-0612551

March 8, 1996

1998US-0006232

January 13, 1998

PATENT-FAMILY:
PUB-NO

PUB-DATE

LANGUAGE

PAGES

MAIN-IPC

US 5910415 A

June 8, 1999

N/A

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C12Q001/68

WO 9417176 A1

August 4, 1994

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C12N005/00

EP 686191 A1

December 13, 1995

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US 5527695 A	June 18, 1996	N/A	027	C12N005/00
US 5744336 A	April 28, 1998	N/A	028	C12N015/00 C07H021/04
APPLICATION-DATA:				
PUB-NO	APPL-DATE	APPL-NO	APPL-DESCRIPTOR	
US 5910415A	January 29, 1993	1993US-0010997	Div ex	
US 5910415A	March 8, 1996	1996US-0612551	Div ex	
US 5910415A	January 13, 1998	1998US-0006232	N/A	
US 5910415A	N/A	US 5527695	Div ex	
US 5910415A	N/A	US 5744336	Div ex	
WO 9417176A1	January 27, 1994	1994WO-US00927	N/A	
EP 686191A1	January 27, 1994	1994EP-0907893	N/A	
EP 686191A1	January 27, 1994	1994WO-US00927	N/A	
EP 686191A1	N/A	WO 9417176	Based on	
US 5527695A	January 29, 1993	1993US-0010997	N/A	
US 5744336A	January 29, 1993	1993US-0010997	Div ex	
US 5744336A	March 8, 1996	1996US-0612551	N/A	
US 5744336A	N/A	US 5527695	Div ex	
INT-CL (IPC): A01H 1/04; A01H 4/00; A01H 5/00; A01H 5/10; C07H 21/04; C12N 5/00; C12N 15/00; C12N 15/09; C12N 15/63; C12N 15/82; C12Q 1/68				
IN: HODGES, T K, LYZNIK, L A				

AB: The following are new: (1) a DNA construct (I) for transforming a eukaryotic cell comprising: (a) a multifunctional DNA sequence comprising: (i) a gene encoding a selectable marker operably linked to (ii) regulatory sequences for eukaryotic gene expression; and (iii) a sequence of interest flanked by (iv) sequences homologous to eukaryotic cell sequences; and (b) a pair of directly repeating site-specific (s-s) recombination sequences; (2) a DNA construct (II) for inserting a DNA sequence of interest into eukaryotic cell DNA comprising a multifunctional DNA sequence comprising: (i) a gene encoding a 1st s-s recombinase capable of recognising 1st s-s recombination sequences; (ii) a DNA sequence targeted for inversion via homologous recombination into eukaryotic cell DNA, comprising a sequence of interest and excisable selection region and flanked by: (iii) a sequence homologous to eukaryotic cell sequences, where the excisable selection region comprises a gene encoding a selectable marker and a gene encoding a 2nd s-s recombinase capable of recognising a 2nd s-s recombination sequence, both genes capable of eukaryotic gene expression, and the excisable region is flanked by: (iv) a pair of directly repeating s-s recombination sequences; and (3) a DNA construct (III) for transforming eukaryotic cells comprising: (a) a multifunctional DNA sequence comprising: (i) a gene encoding a selectable marker operably linked to (ii) regulatory sequences for eukaryotic gene expression; (iii) a DNA sequence targeted for inversion into the eukaryotic cell having less than or equal to 1 polylinker region and flanked by: (iv) nucleotide sequences homologous to eukaryotic cell sequences; and (b) a flanking pair of directly-repeated s-s recombination sequences. Also claimed are: (4) a plant entity comprising a plant cell, seed or plant, produced from the in vitro introduction of an exogenous DNA fragment into a plant cell; (5) a method for directly selecting for insertion of a DNA sequence of interest into a specific sequence of an organism's DNA comprising: (a) introducing (II) into an organism's cells; (b) applying selection means to isolate cells contg. (II) integrated into cellular DNA; (c) removing randomly inserted DNA constructs; (d) applying selection means to isolate cells having the targeted DNA sequence integrated into the organism's DNA via a homologous recombination event; (e) removing the excisable selection region; and (f) culturing the resultant cells to regenerate an entire organism; and (6) a kit contg. (III) and an inducer cpd. capable of inducing an inducible promoter. USE - (I) can be used to target a DNA sequence of interest into a specific site of a host cell's DNA. (II) is useful for directly selecting for insertion of a DNA sequence of interest into a specific sequence of an organism's DNA. Fertile, transgenic plants can be produced (claimed) contg. a DNA sequence of interest, utilising (I), (II) or (III). A method for the production of fertile, transgenic plants wherein the transgenic plant has a DNA sequence of interest integrated at a predetermined DNA sequence of the plant, said method comprising the steps of, introducing into plant cells a DNA construct comprising, a multifunctional DNA sequence flanked by a pair of directly repeated site-specific recombination sequences, said multifunctional DNA sequence comprising a gene encoding a selectable marker, and a DNA sequence of interest, wherein

said DNA sequence of interest is flanked by nucleotide sequences sharing homology to the predetermined nucleotide sequence present in the plant cell, and the selectable marker gene is operably linked to regulatory sequences capable of expressing the gene in the plant cell., selecting for plant cells having said DNA construct integrated into the DNA of the plant cell., eliminating randomly inserted DNA constructs through expression of a recombinase gene capable of initiating recombination at the site-specific recombinase sequences in the plant cells., identifying cells having said DNA sequence of interest integrated into the plant's DNA via a homologous recombination event, and, culturing said identified cells to generate an entire plant., The following are new: (1) a DNA construct (I) for transforming a eukaryotic cell comprising: (a) a multifunctional DNA sequence comprising: (i) a gene encoding a selectable marker operably linked to (ii) regulatory sequences for eukaryotic gene expression; and (iii) a sequence of interest flanked by (iv) sequences homologous to eukaryotic cell sequences; and (b) a pair of directly repeating site-specific (s-s) recombination sequences; (2) a DNA construct (II) for inserting a DNA sequence of interest into eukaryotic cell DNA comprising a multifunctional DNA sequence comprising: (i) a gene encoding a 1st s-s recombinase capable of recognising 1st s-s recombination sequences; (ii) a DNA sequence targeted for inversion via homologous recombination into eukaryotic cell DNA, comprising a sequence of interest and excisable selection region and flanked by: (iii) a sequence homologous to eukaryotic cell sequences, where the excisable selection region comprises a gene encoding a selectable marker and a gene encoding a 2nd s-s recombinase capable of recognising a 2nd s-s recombination sequence, both genes capable of eukaryotic gene expression, and the excisable region is flanked by: (iv) a pair of directly repeating s-s recombination sequences; and (3) a DNA construct (III) for transforming eukaryotic cells comprising: (a) a multifunctional DNA sequence comprising: (i) a gene encoding a selectable marker operably linked to (ii) regulatory sequences for eukaryotic gene expression; (iii) a DNA sequence targeted for inversion into the eukaryotic cell having less than or equal to 1 polylinker region and flanked by: (iv) nucleotide sequences homologous to eukaryotic cell sequences; and (b) a flanking pair of directly-repeated s-s recombination sequences., Also claimed are: (4) a plant entity comprising a plant cell, seed or plant, produced from the in vitro introduction of an exogenous DNA fragment into a plant cell; (5) a method for directly selecting for insertion of a DNA sequence of interest into a specific sequence of an organism's DNA comprising: (a) introducing (II) into an organism's cells; (b) applying selection means to isolate cells contg. (II) integrated into cellular DNA; (c) removing randomly inserted DNA constructs; (d) applying selection means to isolate cells having the targeted DNA sequence integrated into the organism's DNA via a homologous recombination event; (e) removing the excisable selection region; and (f) culturing the resultant cells to regenerate an entire organism; and (6) a kit contg. (III) and an inducer cpd. capable of inducing an inducible promoter., USE - (I) can be used to target a DNA sequence of interest into a specific site of a host

cell's DNA. (II) is useful for directly selecting for insertion of a DNA sequence of interest into a specific sequence of an organism's DNA. Fertile, transgenic plants can be produced (claimed) contg. a DNA sequence of interest, utilising (I), (II) or (III)., The following are new: (1) a DNA construct (I) for transforming a eukaryotic cell comprising: (a) a multifunctional DNA sequence comprising: (i) a gene encoding a selectable marker operably linked to (ii) regulatory sequences for eukaryotic gene expression; and (iii) a sequence of interest flanked by (iv) sequences homologous to eukaryotic cell sequences; and (b) a pair of directly repeating site-specific (s-s) recombination sequences; (2) a DNA construct (II) for inserting a DNA sequence of interest into eukaryotic cell DNA comprising a multifunctional DNA sequence comprising: (i) a gene encoding a 1st s-s recombinase capable of recognising 1st s-s recombination sequences; (ii) a DNA sequence targeted for inversion via homologous recombination into eukaryotic cell DNA, comprising a sequence of interest and excisable selection region and flanked by: (iii) a sequence homologous to eukaryotic cell sequences, where the excisable selection region comprises a gene encoding a selectable marker and a gene encoding a 2nd s-s recombinase capable of recognising a 2nd s-s recombination sequence, both genes capable of eukaryotic gene expression, and the excisable region is flanked by: (iv) a pair of directly repeating s-s recombination sequences; and (3) a DNA construct (III) for transforming eukaryotic cells comprising: (a) a multifunctional DNA sequence comprising: (i) a gene encoding a selectable marker operably linked to (ii) regulatory sequences for eukaryotic gene expression; (iii) a DNA sequence targeted for inversion into the eukaryotic cell having less than or equal to 1 polylinker region and flanked by: (iv) nucleotide sequences homologous to eukaryotic cell sequences; and (b) a flanking pair of directly-repeated s-s recombination sequences., Also claimed are: (4) a plant entity comprising a plant cell, seed or plant, produced from the in vitro introduction of an exogenous DNA fragment into a plant cell; (5) a method for directly selecting for insertion of a DNA sequence of interest into a specific sequence of an organism's DNA comprising: (a) introducing (II) into an organism's cells; (b) applying selection means to isolate cells contg. (II) integrated into cellular DNA; (c) removing randomly inserted DNA constructs; (d) applying selection means to isolate cells having the targeted DNA sequence integrated into the organism's DNA via a homologous recombination event; (e) removing the excisable selection region; and (f) culturing the resultant cells to regenerate an entire organism; and (6) a kit contg. (III) and an inducer cpd. capable of inducing an inducible promoter., USE - (I) can be used to target a DNA sequence of interest into a specific site of a host cell's DNA. (II) is useful for directly selecting for insertion of a DNA sequence of interest into a specific sequence of an organism's DNA. Fertile, transgenic plants can be produced (claimed) contg. a DNA sequence of interest, utilising (I), (II) or (III).

57. Document ID: US 5763240 A, WO 9322443 A1, AU 9341156 A,
JP 07506252 W, EP 672159 A1
L3: Entry 57 of 58

File: DWPI

Jun 9, 1998

DERWENT-ACC-NO: 1993-368802
DERWENT-WEEK: 199830
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TITLE: In vivo homologous sequence targeting in eukaryotic cells - using a
targeting
polynucleotide and recombinase to deliver agents or alter genes

PRIORITY-DATA:
1992US-0939767

September 2, 1992

1992US-0873438

April 24, 1992

1994US-0275916

July 14, 1994

PATENT-FAMILY:
PUB-NO

PUB-DATE

LANGUAGE
PAGES

MAIN-IPC

US 5763240 A

June 9, 1998

N/A

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C12N015/64

WO 9322443 A1

November 11, 1993

E

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C12N015/90

AU 9341156 A

November 29, 1993

N/A

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C12N015/90

JP 07506252 W

July 13, 1995

N/A

027

C12N015/09

EP 672159 A1

September 20, 1995

E

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C12N015/90

APPLICATION-DATA:
PUB-NO

APPL-DATE

APPL-NO

APPL-DESCRIPTOR

US 5763240A

April 24, 1992

1992US-0873438

Cont of

US 5763240A

July 14, 1994

1994US-0275916

N/A

WO 9322443A1

April 23, 1993

1993WO-US03868

N/A

AU 9341156A

April 23, 1993

1993AU-0041156

N/A

AU 9341156A

N/A

WO 9322443

Based on

JP07506252W

April 23, 1993

1993JP-0519421

N/A

JP07506252W

April 23, 1993

1993WO-US03868

N/A

JP07506252W

N/A

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Based on

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April 23, 1993

1993EP-0910780

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INT-CL (IPC): A01K 67/027; A61K 48/00; C12N 5/10; C12N 15/09;
C12N 15/64; C12N 15/90; C12P 19/34;
C12Q 1/68; G01N 33/68

IN: SENA, E P, ZARLING, D A

AB: A method is claimed for targeting and altering, by homologous recombination, a pre-selected target DNA sequence in a eukaryotic cell to make a targeted sequence modification, comprising (a) introducing into at least one eukaryotic cell at least one recombinase and at least one targeting polynucleotide having a homology clamp that corresponds to or is complementary to a preselected target DNA sequence and (b) identifying a eukaryotic cell having a targeted DNA sequence modification at a preselected target DNA sequence. Also claimed are (A) a compsn. for producing a targeted modification of an endogenous DNA sequence, comprising a targeting polynucleotide and a recombinase; (B) a compsn. for producing a targeted sequence modification of a human disease allele; a targeting polynucleotide contg. a corrected sequence a recombinase or an expression polynucleotide that encodes and expresses a recombinase; (C) a kit for therapy, monitoring or prophylaxis of a genetic disease comprising a recombinase and a targeting polynucleotide; (D) a method for treating a disease of an animal harbouring a disease allele, comprising administering a compsn. consisting of: (a) a recombinase or an expression polynucleotide encoding a recombinase and (b) a targeting polynucleotide which produces a sequence modification upon homologous recombination with the disease allele; (E) an animal comprising an allele that has a sequence modification as in (D)., USE/ADVANTAGE - The method can be used to target chemical substits. (e.g. drugs) in a sequence-specific manner in vivo, to correct or to generate genetic mutations in endogenous DNA sequence by homologous recombination and/or gene conversion or to produce homologously targeted transgenic animals

at high efficiency. In partic., the method can be used for correcting disease alleles involved in human genetic diseases such as inherited genetic disease (e.g. cystic fibrosis) and neoplasm for treating or preventing viral diseases, by HBV hepatitis.

A method is claimed for targeting and altering, by homologous recombination, a pre-selected target DNA sequence in a eukaryotic cell to make a targeted sequence modification, comprising (a) introducing into at least one eukaryotic cell at least one recombinase and at least one targeting polynucleotide having a homology clamp that corresponds to or is complementary to a preselected target DNA sequence and (b) identifying a eukaryotic cell having a targeted DNA sequence modification at a preselected target DNA sequence. Also claimed are (A) a compsn. for producing a targeted modification of an endogenous DNA sequence, comprising a targeting polynucleotide and a recombinase; (B) a compsn. for producing a targeted sequence modification of a human disease allele; a targeting polynucleotide contg. a corrected sequence a recombinase or an expression polynucleotide that encodes and expresses a recombinase; (C) a kit for therapy, monitoring or prophylaxis of a genetic disease comprising a recombinase and a targeting polynucleotide; (D) a method for treating a disease of an animal harbouring a disease allele, comprising administering a compsn. consisting of: (a) a recombinase or an expression polynucleotide encoding a recombinase and (b) a targeting polynucleotide which produces a sequence modification upon homologous recombination with the disease allele; (E) an animal comprising an allele that has a sequence modification as in (D)., USE/ADVANTAGE - The method can be used to target chemical substituents (e.g. drugs) in a sequence-specific manner in vivo, to correct or to generate genetic mutations in endogenous DNA sequence by homologous recombination and/or gene conversion or to produce homologously targeted transgenic animals at high efficiency. In partic., the method can be used for correcting disease alleles involved in human genetic diseases such as inherited genetic disease (e.g. cystic fibrosis) and neoplasm for treating or preventing viral diseases, by HBV hepatitis.

58. Document ID: EP 542466 A2, AU 655512 B, AU 9228316 A, CA 2082577 A, EP 542466 A3, JP 05336977 A, NZ 245070 A, ZA 9208662 A
L3: Entry 58 of 58

File: DWPI

May 19, 1993

DERWENT-ACC-NO: 1993-160938
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TITLE: Baculovirus transfer vector contg. locus of crossover PI sequence - as substrate for recombinase enzyme, provides efficient homologous recombination with recombinant virus, esp. for expression of polypeptide(s) for vaccines

PRIORITY-DATA:

1991GB-0023929

November 11, 1991

PATENT-FAMILY:
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MAIN-IPC

EP 542466 A2

May 19, 1993

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AU 655512 B

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May 13, 1993

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EP 542466 A3

October 6, 1993

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APPL-NO

APPL-DESCRIPTOR

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November 10, 1992

1992AU-0028316

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AU 9228316

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AU 9228316A

November 10, 1992

1992AU-0028316

N/A

CA 2082577A

November 10, 1992

1992CA-2082577

N/A

EP 542466A3

November 4, 1992

1992EP-0310085

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JP05336977A

November 10, 1992

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NZ 245070A

November 10, 1992

1992NZ-0245070

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ZA 9208662A

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1992ZA-0008662

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INT-CL (IPC): A61K 39/00; A61K 39/12; C12N 0/00; C12N 5/10; C12N 7/01; C12N 15/64; C12N 15/74; C12N 15/86; G01N 33/53

IN: GEWERT, D R, PEAKMAN, T C

AB: New baculovirus transfer vector contains a restriction site for insertion of a

DNA sequence (I) encoding a heterologous polypeptide (II); regulatory elements for

expression of (I) when inserted and a loXP (locus of crossover PI) DNA sequence (III) to

act as substrate for the Cre (causes recombination) recombinase protein (N)., Also new are

(1) recombinant DNA (V) comprising this vector and (I); (2) a baculovirus contg. (III) as

substrate for (IV); (3) recombinant baculovirus prepd. by homologous recombination of the

virus (2) and (V); (4) insect cells transfected with the recombinant virus; (5) vaccines

contg. (II) prepd. by culturing the transfected insect cells; and (6) test kits for

detecting (II)-specific antibodies or (II) themselves., (III) is esp. of formula,

5'-CCTTAATATAACTTCGTATAP

TGTATGCTATACGAAGTTATTAGGTCG 3'-GGAATTATATTGA AGCATATTACA

TACGATATGCTTCAATAATCCAGC, USE/ADVANTAGE - The transfected cells provide high level

expression of (II) which are useful in human or veterinary medicine; in vaccines and in

diagnostic assays. The transfer vector provides an efficient in vitro system for

constructing recombinant viruses which can be identified and isolated. Up to 50 million

recombinants can be produced from 1 microg plasmid DNA and up to 50% of viral progeny are

recombinants. If required inserted genes are easily recovered and reinserted, and

recombination efficiency is independent of gene size (which can be 10kb or larger).